Cell Injury

Subject : G. Pathology

Introduction

- *Cell injury is defined as a variety of stresses a cell encounters as a result of changes in its internal and external environment.*
- **Virchow's Cellular theory of disease** (1859): diseases occur due to abnormalities at the level of cells
- The cellular response to stress may vary and depends upon the following:
  - The type of cell and tissue involved.
  - Extent and type of cell injury

ETIOLOGY OF CELL INJURY

Genetic causes

- *Developmental defects:* Errors in morphogenesis
- *Cytogenetic (Karyotypic) defects:* chromosomal abnormalities
- *Single-gene defects:* Mendelian disorders
- *Multifactorial inheritance disorders*

Acquired causes

- Hypoxia and ischaemia
- Physical agents
- Chemical agents and drugs
- Microbial agents
- Immunologic agents
- Nutritional derangements
- Aging
- Psychogenic diseases
- Iatrogenic factors
- Idiopathic diseases.

Acquired causes

Oxygen deprivation

HYPOXIA

- **Ischemia** (loss of blood supply).
- Inadequate oxygenation (cardiorespiratory failure).
- Loss of oxygen carrying capacity of the blood (anemia or CO poisoning).

HYPOXIC INJURY

- Loss of oxidative phosphorylation and ATP generation by mitochondria.
- Decreased ATP (with increase in AMP): stimulating fructokinase and phosphorylation, resulting in aerobic glycolysis.
- Depleted glycogen.
- Reduced intracellular pH: Lactic acid and inorganic phosphate.
- Clumping of nuclear chromatin.

PHYSICAL AGENTS

- Trauma
- Heat
- Cold
- Radiation
- Electric shock

CHEMICAL AGENTS AND DRUGS

- Endogenous products: urea
- Exogenous agents
  - Therapeutic drugs: hormones
  - Nontherapeutic agents: lead or alcohol

FREE RADICAL INITIATION

- Absorption of energy (UV light and x-rays)
- Oxidative metabolic reactions
- Enzymatic conversion of exogenous chemicals or drugs ($CCl_4 > CCl_3\cdot$)
- Oxygen-derived radicals
- Superoxide

INFECTIOUS AGENTS

- Viruses
- Rickettsiae
- Bacteria
- Fungi
- Parasites

Abnormal immunological reactions

The immune process is normally protective but in certain circumstances the reaction may become deranged.

- Hypersensitivity to various substances can lead to anaphylaxis or to more localized lesions such as asthma.
- In other circumstances the immune process may act against the body cells - autoimmunity.

Nutritional imbalances

- Protein-calorie deficiencies are the most examples of nutrition deficiencies.
- Vitamins deficiency.
- Excess in nutrition are important causes of morbidity and mortality.
- Excess calories and diet rich in animal fat are now strongly implicated in the development of atherosclerosis.
- Obesity alone leads to an increased vulnerability to certain disorders, such as atherosclerosis, coronary heart disease, diabetes mellitus

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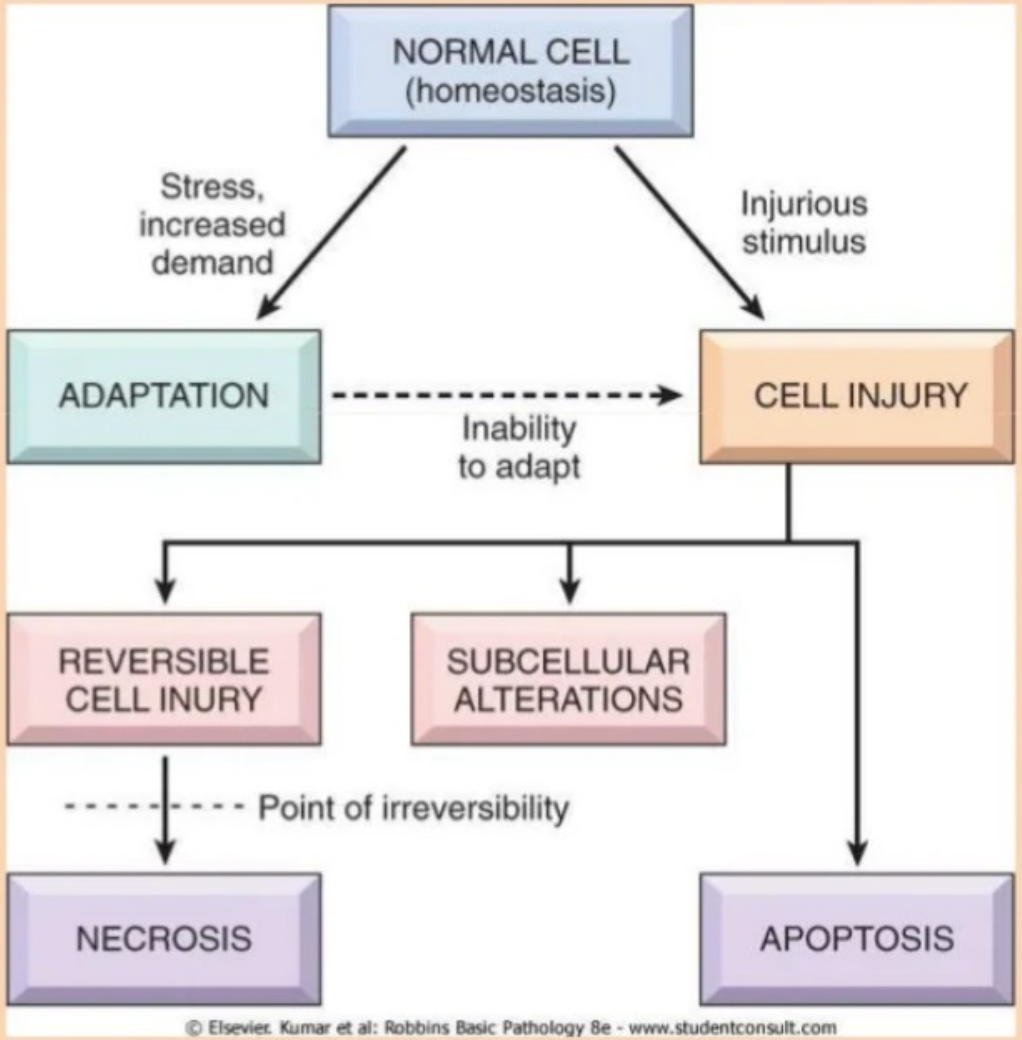
Aging

- Programmed aging whereby after a defined number of divisions the cell undergoes terminal differentiation.
- Development of an increasing population of cells irreversibly committed to senescence and death.
- Increased susceptibility to somatic mutation and a build-up of errors leading to an eventual' error catastrophe.
- Faulty DNA repair mechanisms.

CELLS REACT TO ADVERSE INFLUENCES

- **Cellular adaptation**
  1. Hyperplasia
  2. Hypertrophy
  3. Atrophy
  4. Metaplasia
  5. Dysplasia
- **Reversible injury**
  1. intracellular edema,
  2. fatty change,
  3. hyaline change,
  4. amyloidosis,
  5. mucoid degeneration,
  6. pathologic pigments
- **Irreversible injury and dying:** Necrosis, Gangrene followed by pathological calcification

CELLULAR RESPONSE TO ADVERSE EFFECT



CELLULAR ADAPTATION

Cellular ADAPTATION

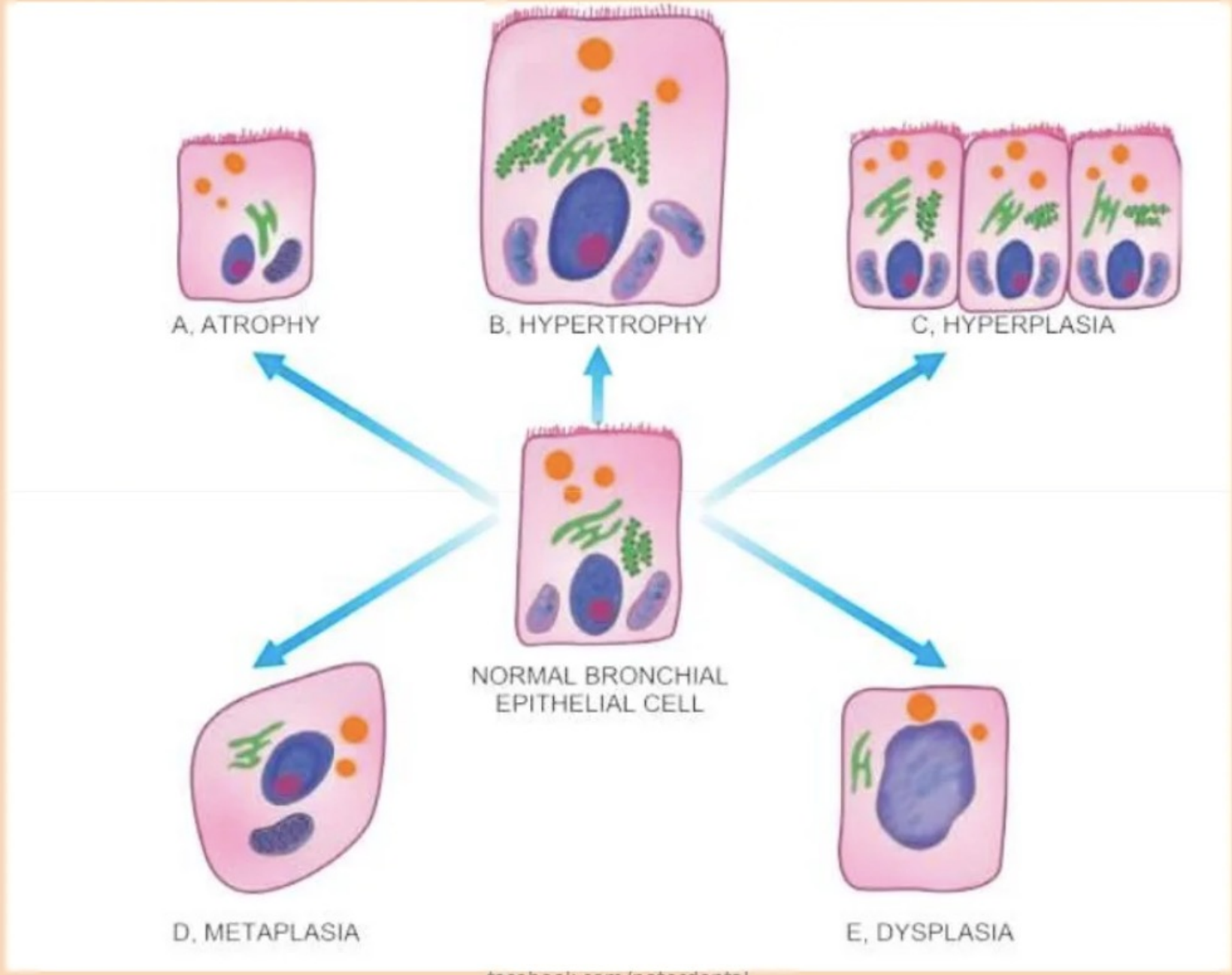
- *Adaptations are reversible changes in the size, number, phenotype, metabolic activity, or functions of cells in response to changes in their environment*
- Cells must constantly adapt, even under normal conditions, to changes in their environment.
- These physiological adaptations usually represent responses of cells to normal stimulation by hormones or endogenous chemical substances.
  - For example, as in the enlargement of the breast and induction of lactation by pregnancy.

Types of Adaptation

- Pathologic adaptations may share the same underlying mechanisms, but they provide the cells with the ability to survive in their environment and perhaps escape injury.
- Cellular adaptation is a state that lies intermediate between the normal, unstressed cell and the injured, overstressed cell.

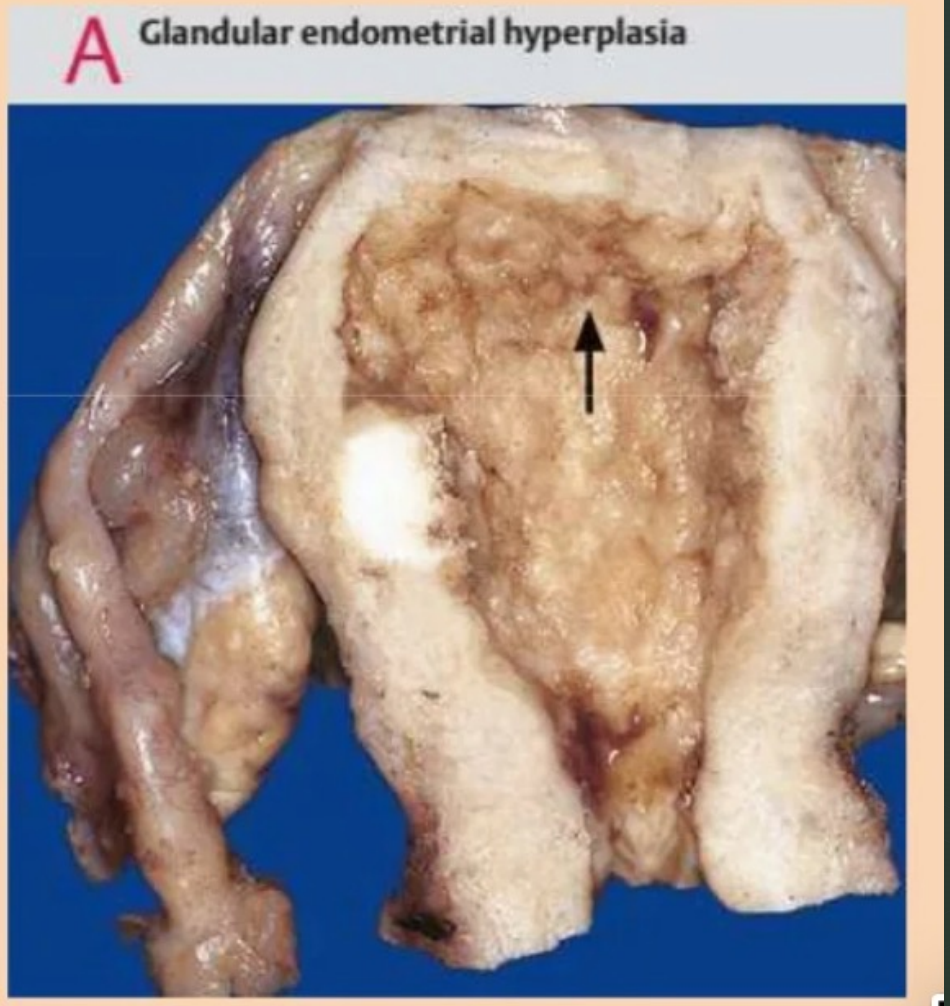
Cellular Adaptation

- Cell can adapt themselves by undergoing 5 different conditions
  1. Hyperplasia
  2. Hypertrophy
  3. Atrophy
  4. Metaplasia
  5. Dysplasia


A. ATROPHY
B. HYPERTROPHY
C. HYPERPLASIA
NORMAL BRONCHIAL
EPITHELIAL CELL
D. METAPLASIA
E. DYSPLASIA

Hyperplasia

An increase in the number of cells in an organ or tissue, which may then have increased volume.



Types of Hyperplasia : Physiological

a. Hormonal : influence of hormonal stimulation
   - hyperplasia of the female breast epithelium at puberty or in pregnancy.
   - pregnant uterus
   - normal endometrium after a normal menstrual cycle.
   - Prostatic hyperplasia in old age

b. Compensatory: hyperplasia occurring following removal of part of an organ or a contralateral organ in paired organ
   - Regeneration of the liver following partial hepatectomy
   - Regeneration of epidermis after skin abrasion
   - Following nephrectomy on one side, there is hyperplasia of nephrons of the other kidney.

Types of Hyperplasia : Pathological

- Excessive stimulation of hormones or growth factors
  - Endometrial hyperplasia
  - wound healing - of granulation tissue due to proliferation of fibroblasts and endothelial cells.
  - skin warts from hyperplasia of epidermis due to human papilloma virus.
  - Pseudocarcinomatous hyperplasia of the skin

Hypertrophy

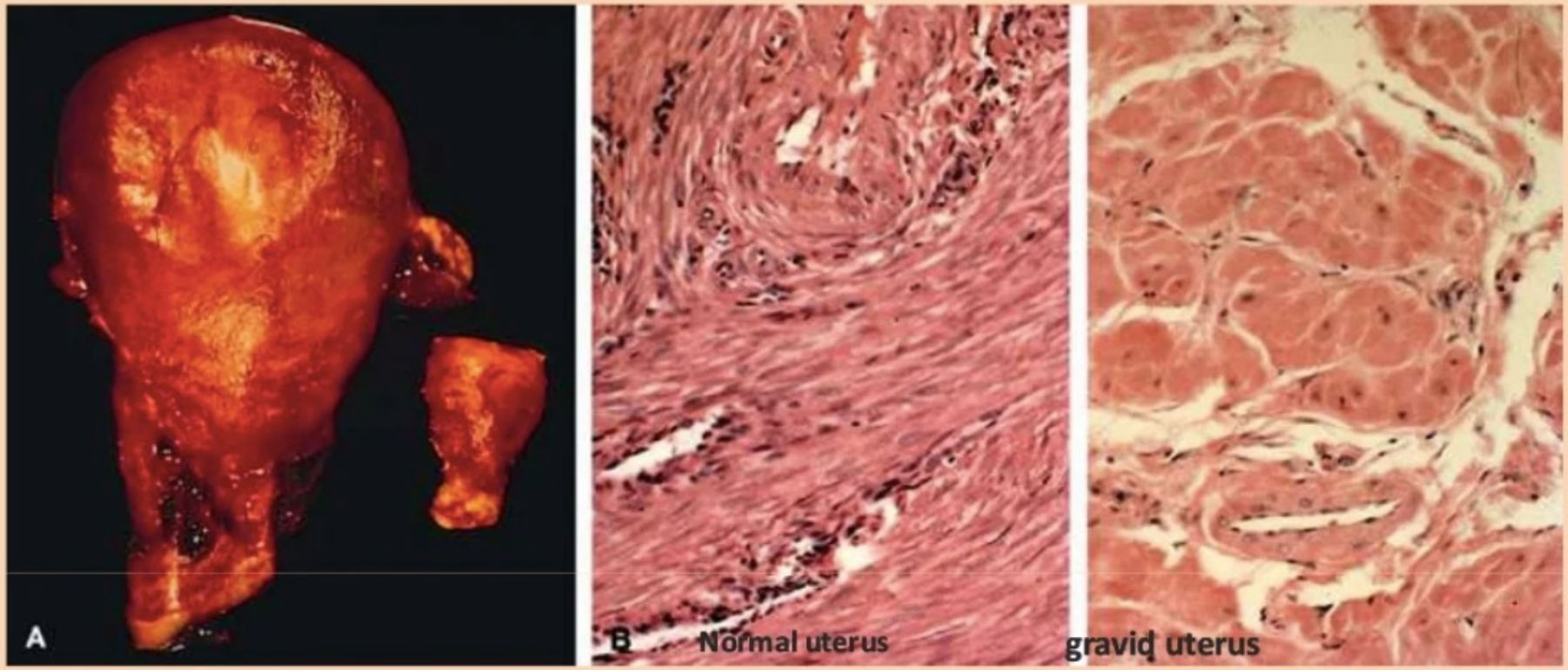
Definition: An increase in the size of cells, and with such change, an increase in the size of the organ.

Types:

- ***Physiologic:*** physiologic growth of the uterus during pregnancy involves both hypertrophy and hyperplasia.
- **Pathologic causes:** increased workload, hormonal stimulation and growth factors stimulation.
  - hypertrophy of heart the most common stimulus is chronic hemodynamic overload

Hypertrophied heart

（From ROBBINS BASIC PATHOLOGY，2003）



Physiologic hypertrophy of the uterus during pregnancy.A, gross appearance of a normal uterus (right) and a gravid uterus (left) that was removed for postpartum bleeding,

（From ROBBINS BASIC PATHOLOGY，2003）

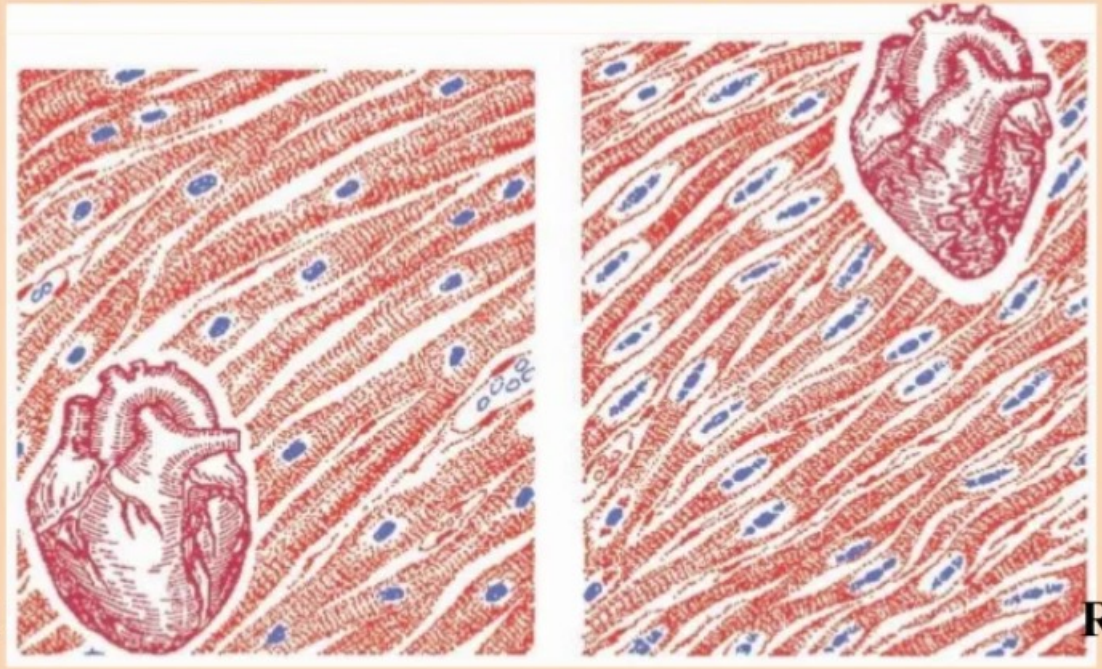
The relationship between hyperplasia and hypertrophy:

Although hypertrophy and hyperplasia are two distinct processes, frequently both occur together, and they well be triggered by the same mechanism.

Atrophy

Definition: Acquired loss of size due to reduction of cell size or number of parenchyma cells in an organ

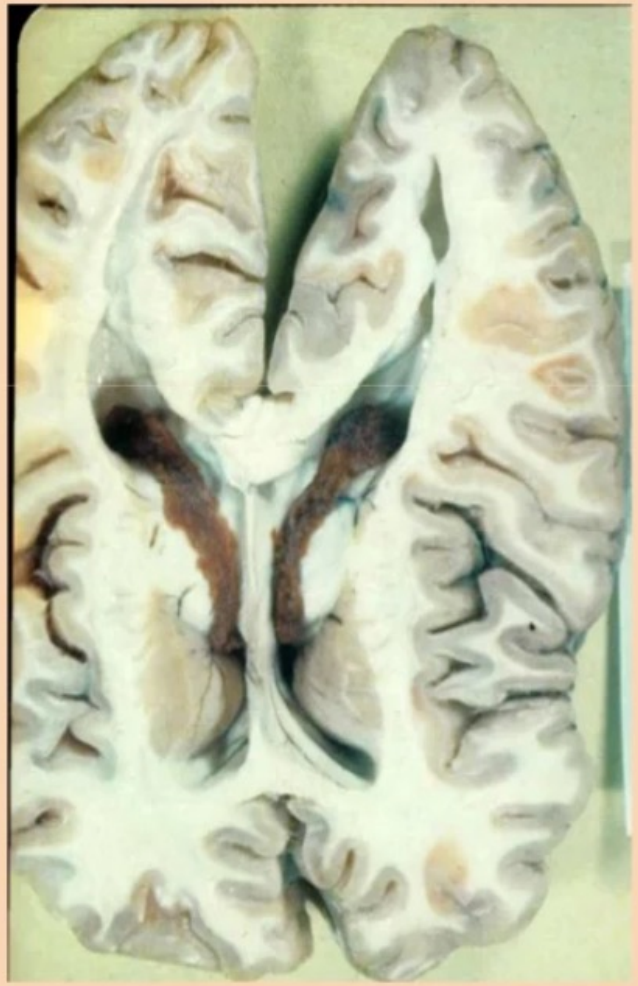
Types: **Physiological or Pathological**



Left Normal **Right Atrophy**

Physiologic atrophy

- A normal process of aging in some tissues, which could be due to loss of endocrine stimulation or arteriosclerosis.
  - Atrophy of **lymphoid** tissue in lymph nodes, appendix and thymus.
  - Atrophy of **gonads** after **menopause**.
  - Atrophy of **brain** with **aging**.



Pathologic atrophy.

- Starvation atrophy.
- Ischaemic atrophy
- Disuse atrophy.
- Neuropathic atrophy.
- Endocrine atrophy
- Pressure atrophy.
- Idiopathic atrophy

Metaplasia

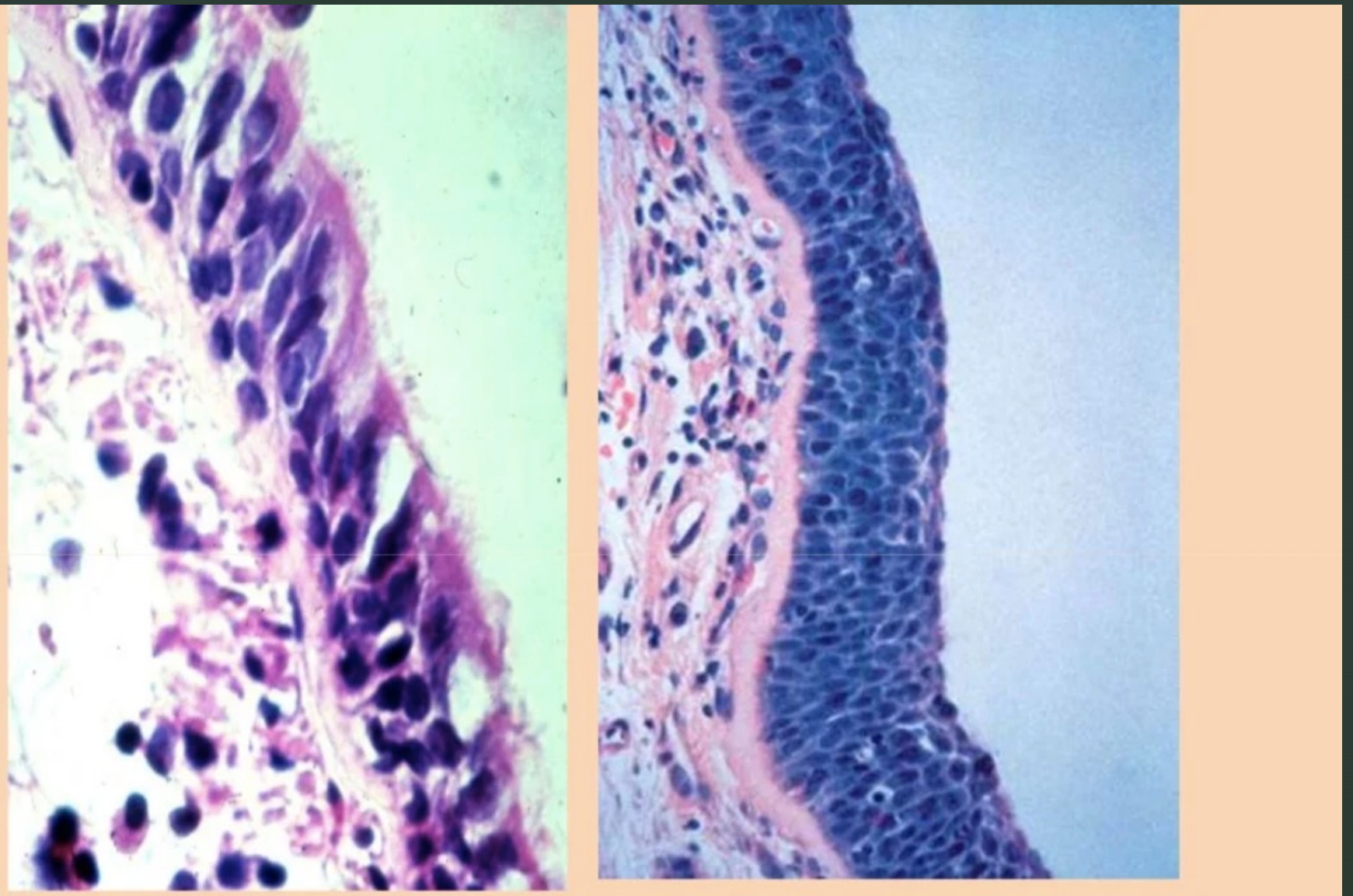
Definition: Metaplasia is a reversible change in which one adult cell type is replaced by another adult cell type.

Causes

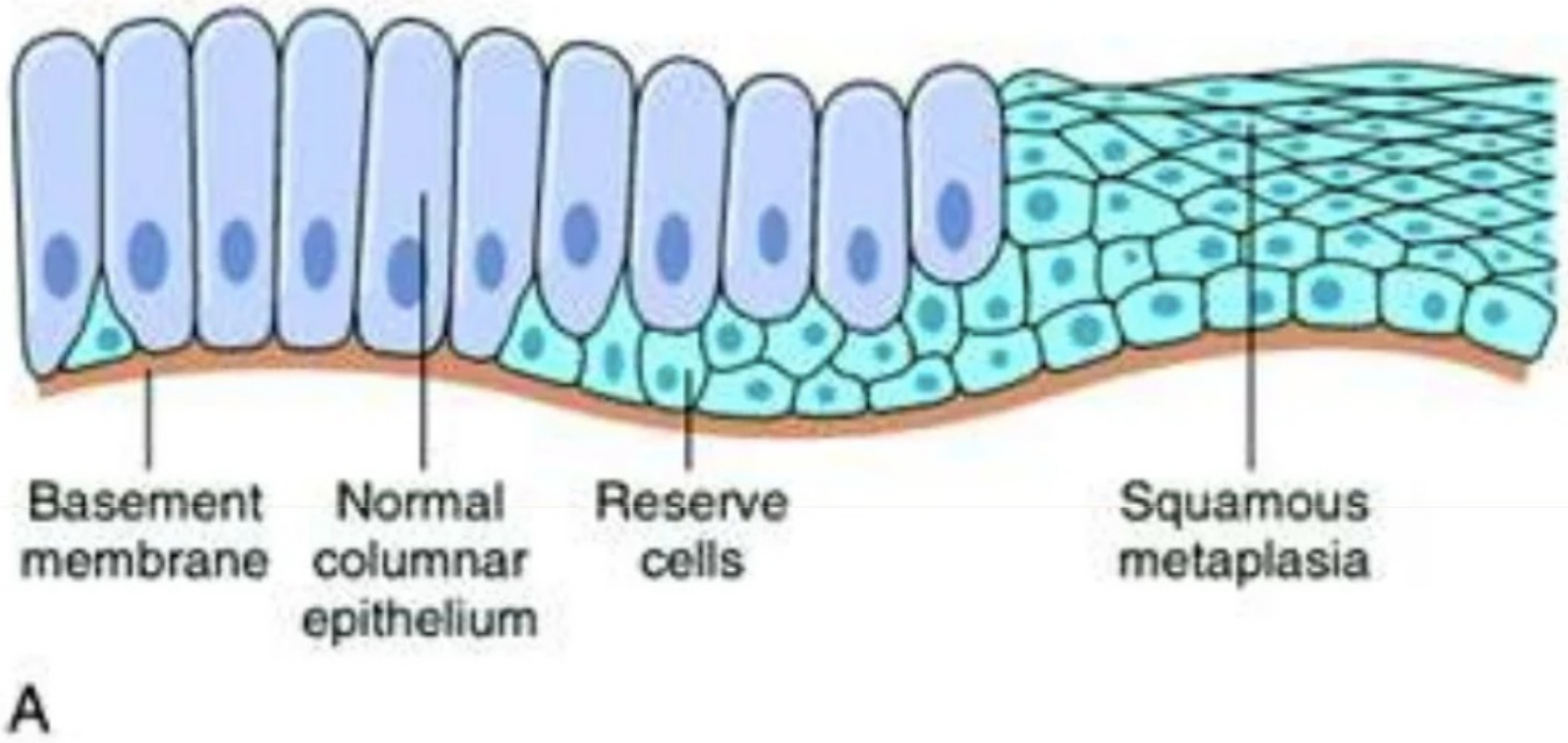
- Changes in environment
- Irritation or inflammation
- Nutritional

Types of Metaplasia

- There are basically 2 types of metaplasia
- **EPITHELIAL METAPLASIA**
  - **Squamous metaplasia:** changes in bronchus, uterine endocervix, gallbladder, prostate, renal pelvis and urinary bladder
    - *vitamin A deficiency:* squamous metaplasia in the nose, bronchi, urinary tract, lacrimal and salivary glands
  - **Columnar metaplasia:** Intestinal metaplasia in healed chronic gastric ulcer and Barrett's oesophagus
- **MESENCHYMAL METAPLASIA**
  - **Osseous metaplasia.**
  - **Cartilaginous metaplasia.**



Squamous metaplasia in bronchitis



Schematic diagram of columnar to squamous metaplasia

（From ROBBINS BASIC PATHOLOGY，2003）

DYSPLASIA

- disordered cellular development.
- also referred to as *atypical hyperplasia*
- Epithelial dysplasia is characterised by cellular proliferation and cytologic changes
  - Increased number of layers of epithelial cells
  - Disorderly arrangement of cells from basal layer to the surface layer
  - Loss of basal polarity i.e. nuclei lying away from basement membrane
  - Cellular and nuclear pleomorphism
  - Increased nucleocytoplasmic ratio
  - Nuclear hyperchromatism
  - Increased mitotic activity.
- The two most common examples of dysplastic changes are the uterine cervix and respiratory tract

Differences between Metaplasia and Dysplasia.

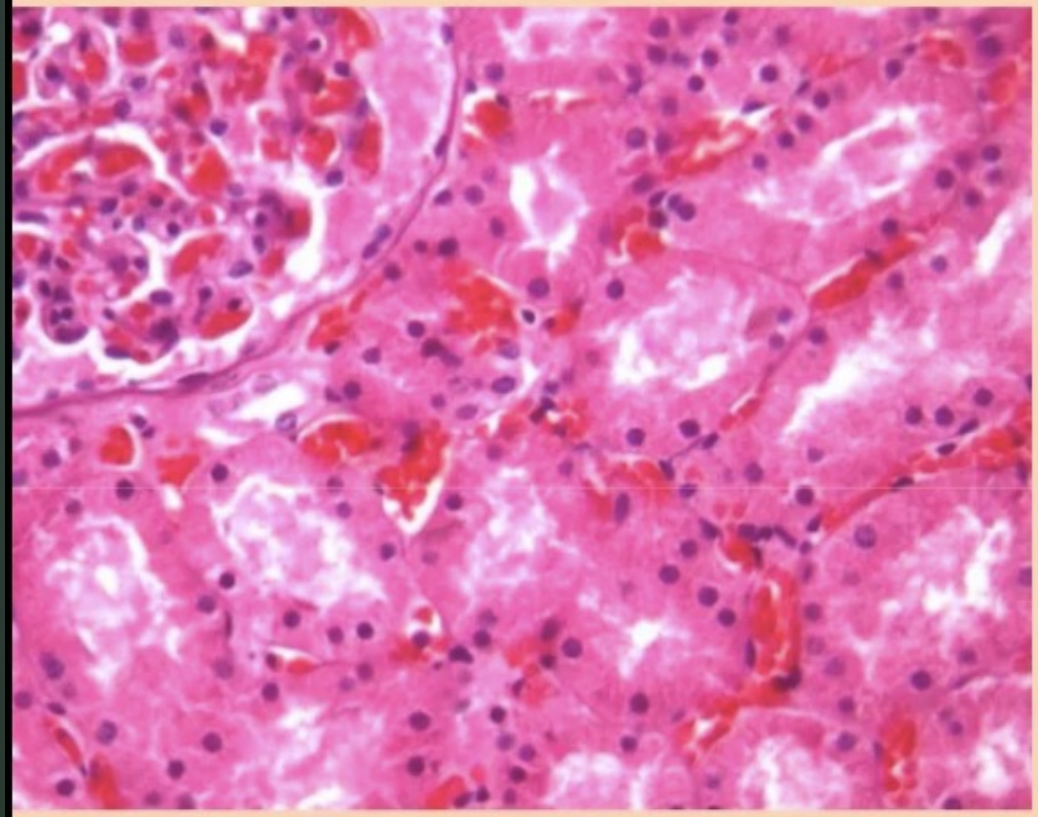
ature	Metaplasia	Dysplasia
Definition	Change of one type of epithelial or mesenchymal cell to another type of adult epithelial or mesenchymal cell	Disordered cellular development, may be accompanied with hyperplasia or metaplasia
Types	Epithelial (squamous, columnar) and mesenchymal (osseous, cartilaginous)	Epithelial only
Tissues affected	Most commonly affects bronchial mucosa, uterine endocervix; others mesenchymal tissues (cartilage, arteries)	Uterine cervix, bronchial mucosa
Cellular changes	Mature cellular development	Disordered cellular development (pleomorphism, nuclear hyperchromasia, mitosis, loss of polarity)
Natural history	Reversible on withdrawal of stimulus	May regress on removal of inciting stimulus, or may progress to higher grades of dysplasia or carcinoma *in situ*

Reversible Injury

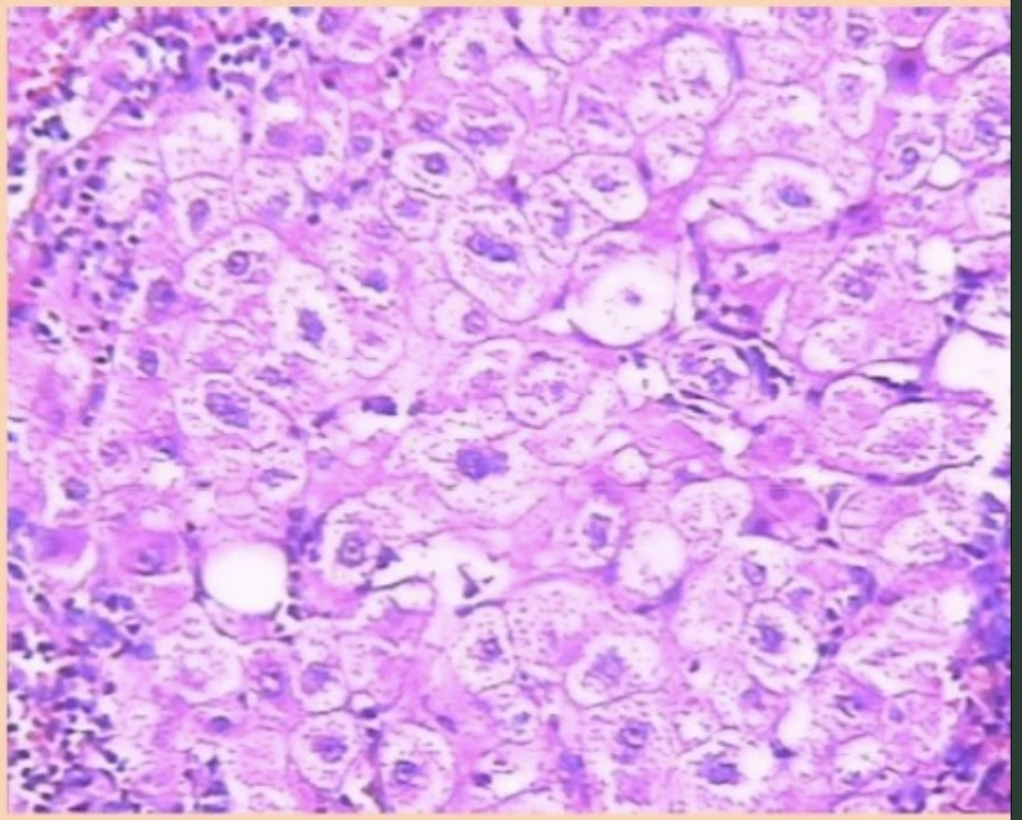
- Intracellular edema,
- Fatty change,
- Hyaline change,
- Amyloidosis,
- Mucoid Degeneration,
- Pathologic Pigments

Intracellular edema

- Also known as **cloudy swelling**.
- Accumulation of watery fluid in cells.
- Commonest and earliest form of cell injury
- Caused by bacterial toxins, chemicals, poisons, burns, high fever, intravenous administration of hypertonic glucose or saline.
- Impaired regulation of sodium and potassium at the level of cell membrane.
- **Morphologic change**
  - **Gross features**: cloudy swelling
  - **M/S Changes**: Parenchymal cells swollen.



Left Granularity change in kidney



Right Hydropic change

Fatty change

Definition: There is the accumulation of fat in non-fatty cells.

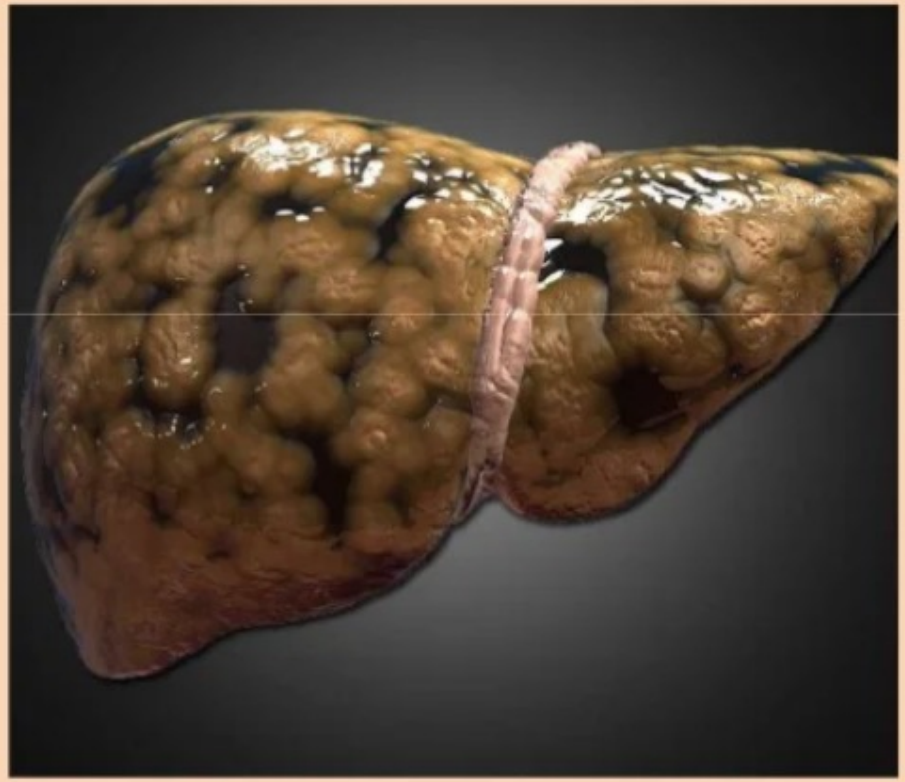
- Also known as **steatosis**

Morphologic change:

- Gross features: The organ enlarges and becomes yellow, soft, and greasy.
- M/S: An Fatty change appears as clear vacuoles within parenchymal cells.

Fatty change: Liver

- Since this organ plays a central role in fat metabolism,
- The accumulation of fat in toxic conditions can be very dangerous.
- Depending upon the cause and amount of accumulation, fatty change may be
  - mild and reversible,
  - or severe producing irreversible cell injury and cell death

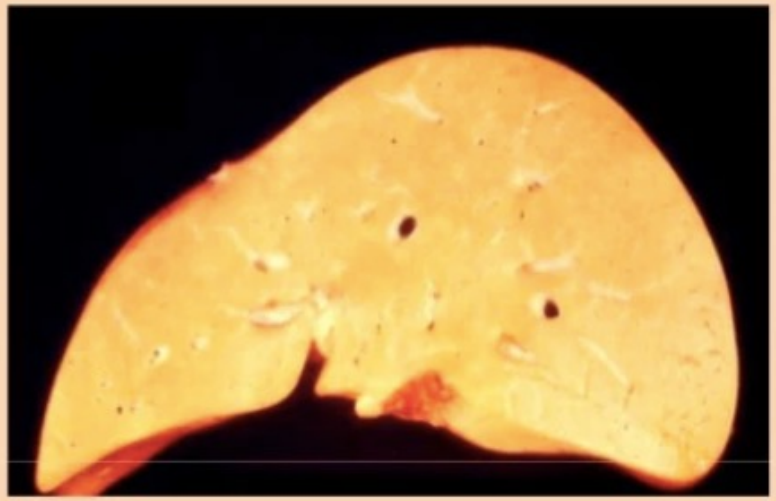


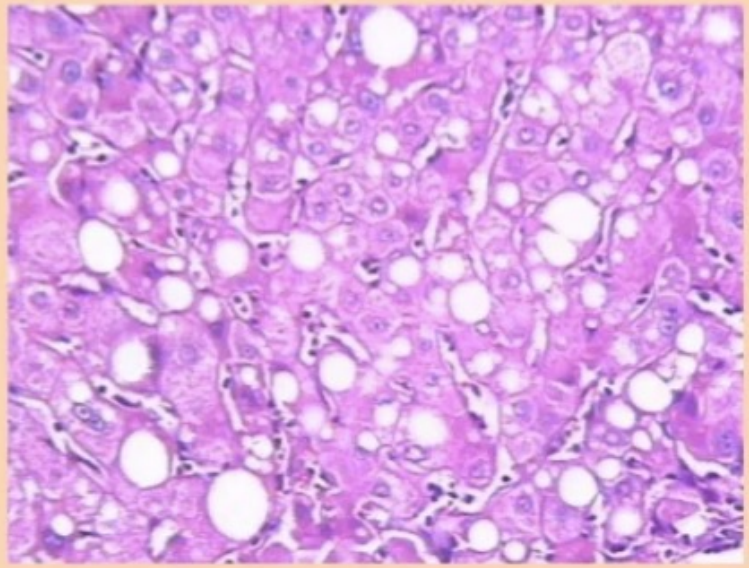
Etiology

- **Conditions with excess fat**
  - Obesity
  - Diabetes mellitus
  - Congenital hyperlipidaemia
- **Liver cell damage:**
  - Alcoholic liver disease (most common)
  - Starvation
  - Protein calorie malnutrition
  - Chronic illnesses (e.g. tuberculosis)
  - Acute fatty liver in late pregnancy
  - Hypoxia (e.g. anaemia, cardiac failure)
  - Hepatotoxins (e.g. carbon tetrachloride, chloroform, ether, aflatoxins and other poisons)
  - Drug-induced liver cell injury (e.g. administration of methotrexate, steroids, CCl4, halothane anaesthetic, tetracycline etc)
  - Reye's syndrome

MORPHOLOGIC FEATURES

- **Grossly**
  - the liver in fatty change is enlarged with a tense, glistening capsule and rounded margins.
  - The cut surface bulges slightly and is pale-yellow to yellow and is greasy to touch
- **Microscopically**
  - characteristic feature is the presence of numerous lipid vacuoles in the cytoplasm of hepatocytes.





Fatty change: Heart

- It occurs in two patterns,
- **Prolonged moderate hypoxia** causes intracellular deposits of fat,
  - grossly apparent bands of yellowed myocardium alterations with bands of darker, red-brown, uninvolved myocardium (tigered effect).
- **Profound hypoxia** or diphtheritic myocarditis, the myocardial cells are **uniformly affected**.

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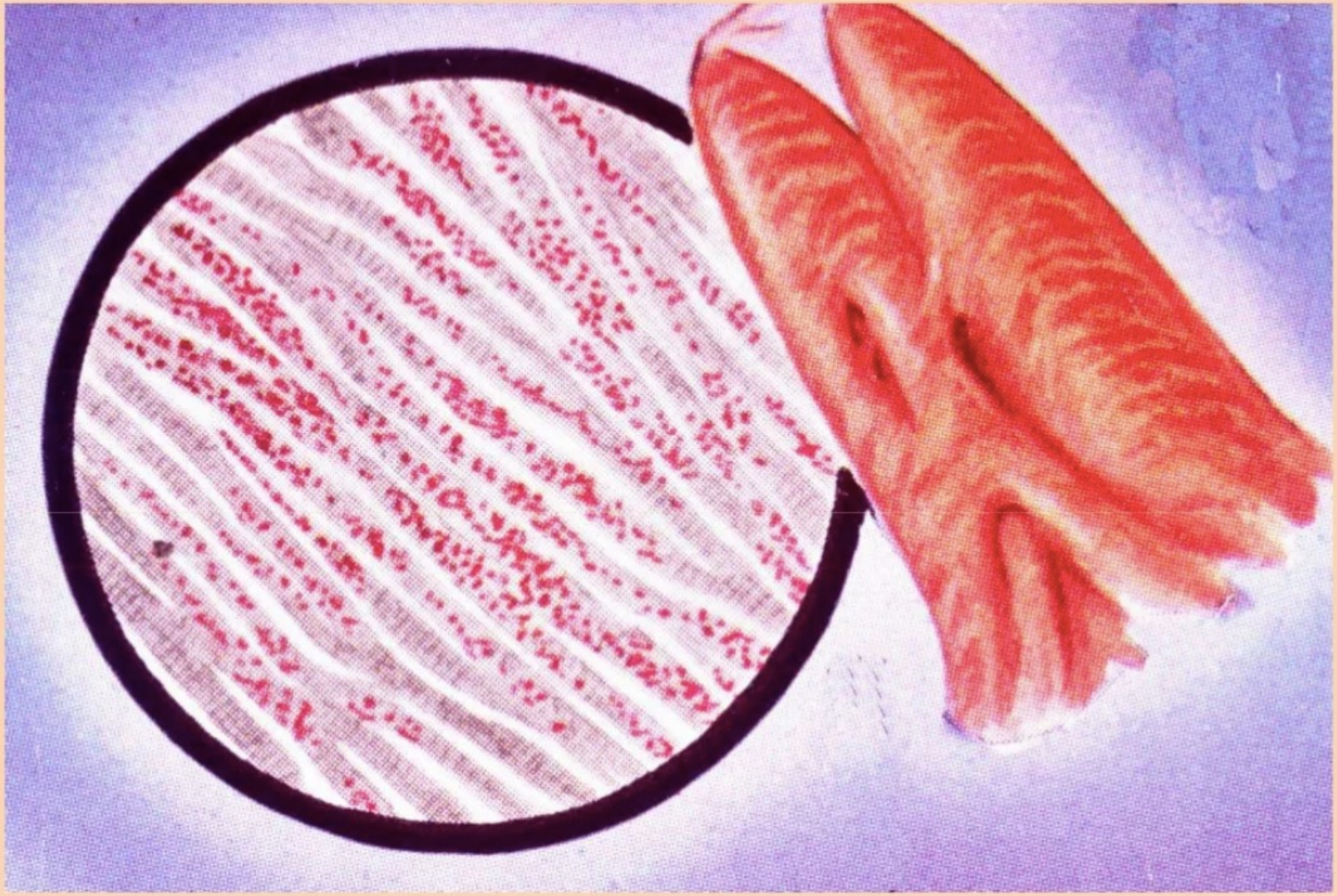

tigered effect

Prof. （From CIBA PHARMACEUTICAL PRODUCTS, INC. 1948） Orr

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Fatty change: Kidney

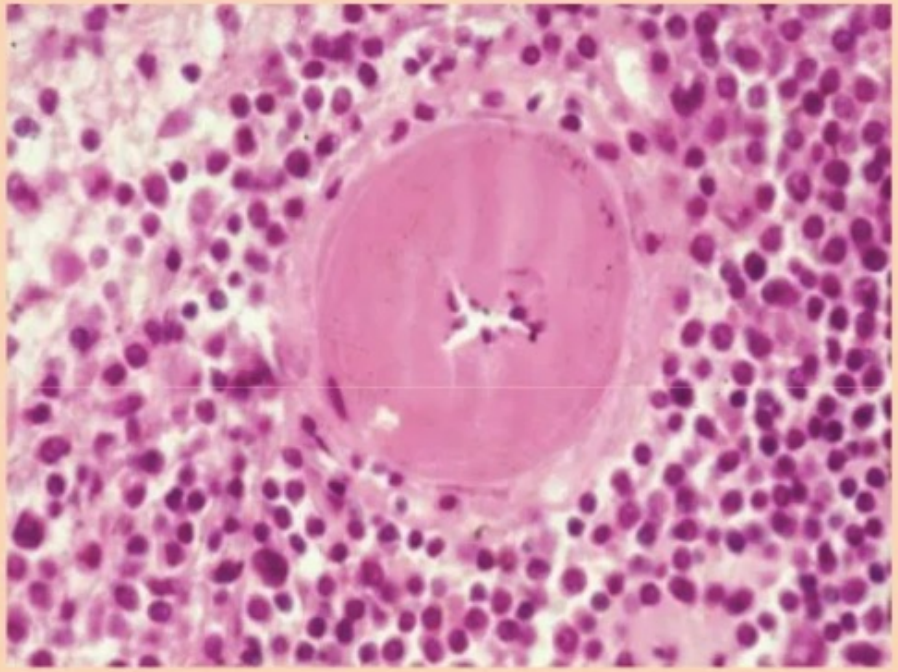
- In most cases fatty change is confined to the epithelium of the convoluted tubules,
- but in severe poisoning it may affect all structures including the glomerule.

Causes:

- Poisons. e. g. carbon tetrachloride, phosphorus (liver)
- Chronic alcoholism (liver)
- Infections
- Congestive cardiac failure
- Severe anaemia
- Ischaemia
- Diabetes mellitus
- Malnutrition and wasting disease.

Hyaline change

- Not a distinct chemical entity.
- Various histological or cytological alterations characterized by **homogeneous, glasslike** appearance in hematoxylin and eosin-stained sections.
- It may be intracellular or extracellular.

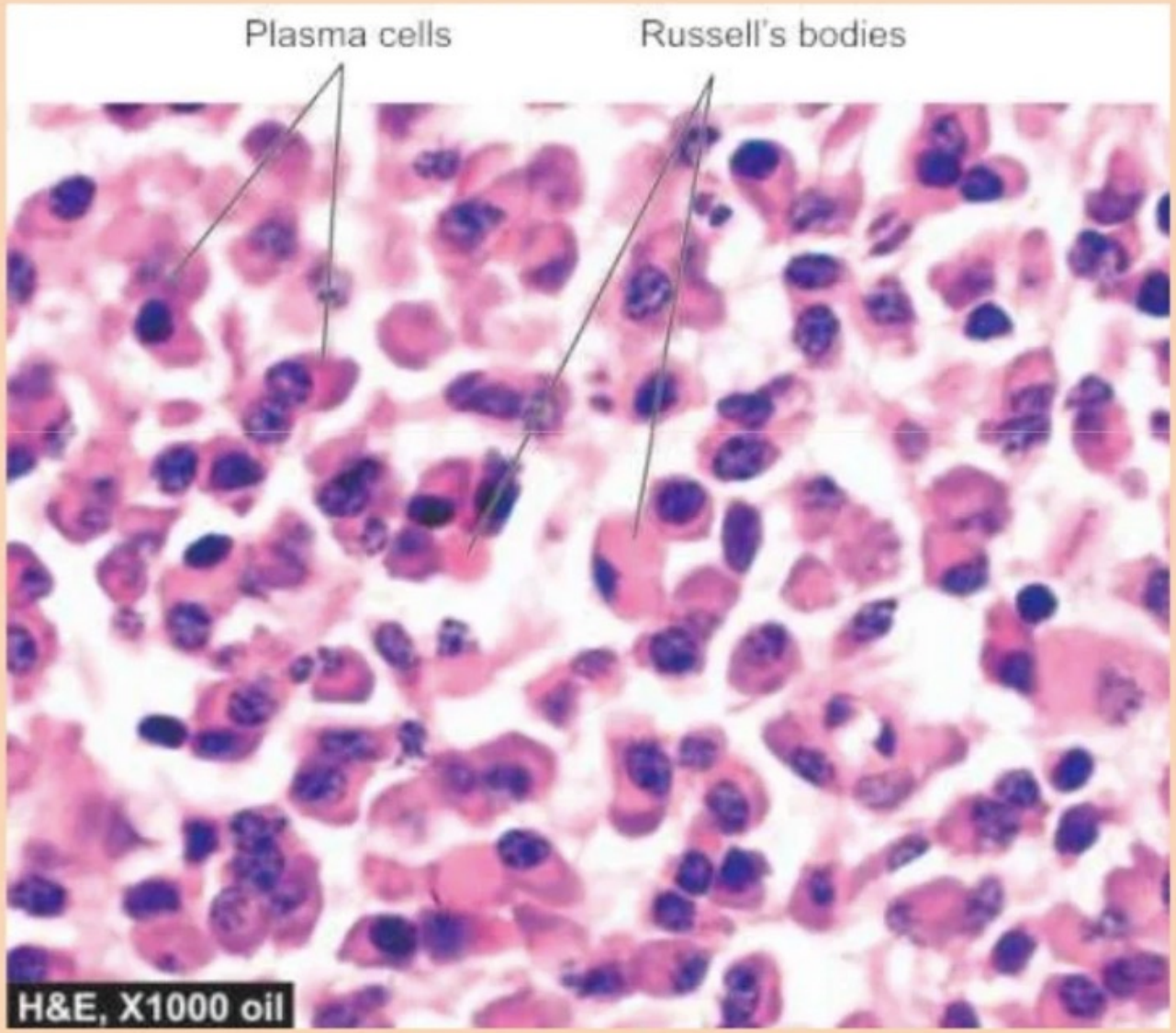


Hyalinization Arteriolar Sclerosis

INTRACELLULAR HYALINE

- Its mainly seen in epithelial cells.
- ***Hyaline droplets*** in the **proximal tubular epithelial cells**: excessive reabsorption of plasma proteins.
- *Hyaline degeneration* of **rectus abdominalis** muscle called **Zenker's degeneration**, occurring in **typhoid fever**.
- ***Mallory's hyaline*** represents aggregates of intermediate filaments in the **hepatocytes** in **alcoholic liver** cell injury.
- Nuclear or **cytoplasmic *hyaline*** *inclusions* seen in some **viral infections**.
- ***Russell's bodies*** representing excessive immunoglobulins in the rough endoplasmic reticulum of the plasma cells

INTRACELLULAR HYALINE

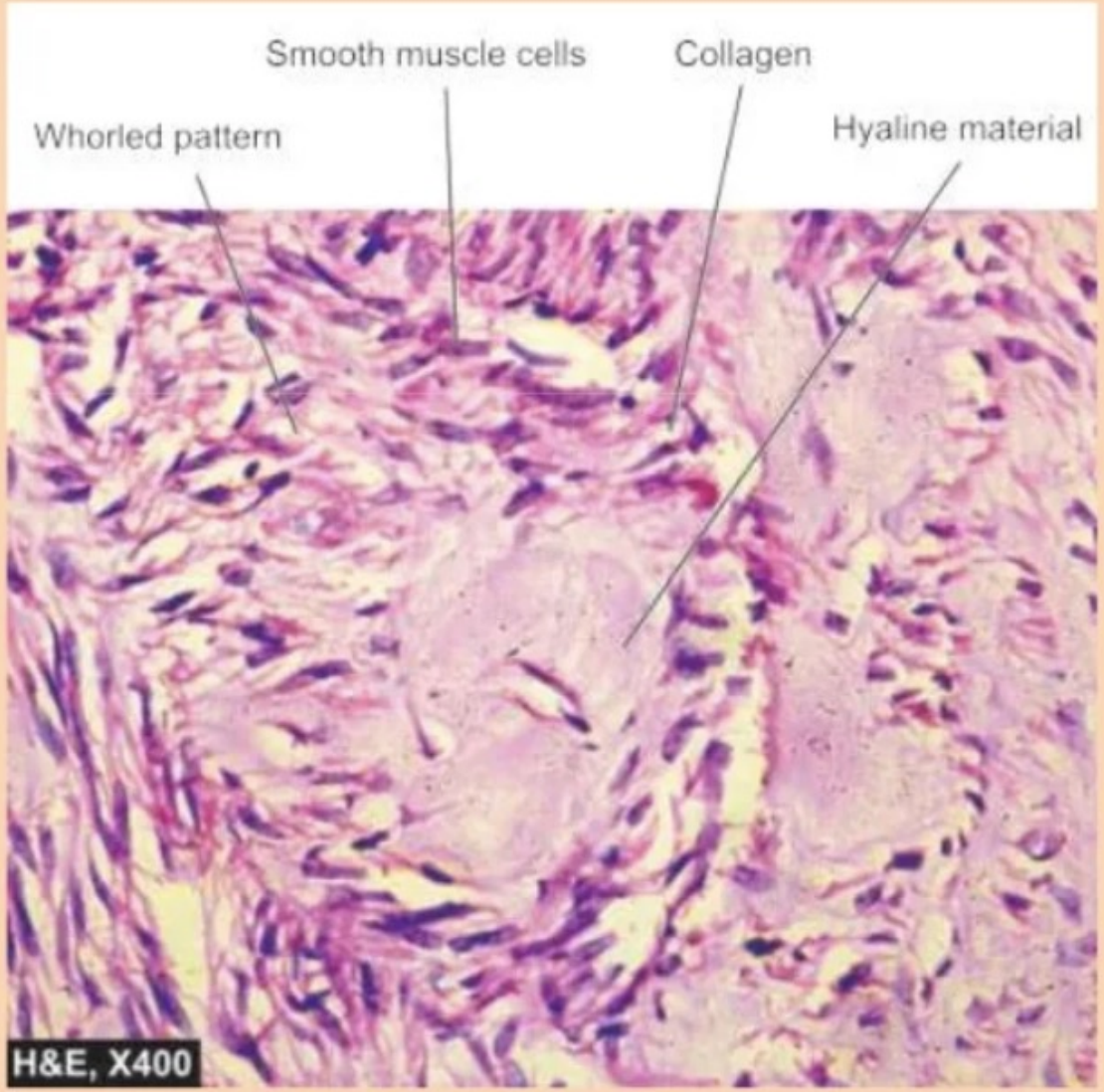


Intracellular hyaline as Russell's bodies in the plasma cells. The cytoplasm shows pink homogeneous globular material due to accumulated immunoglobulins.

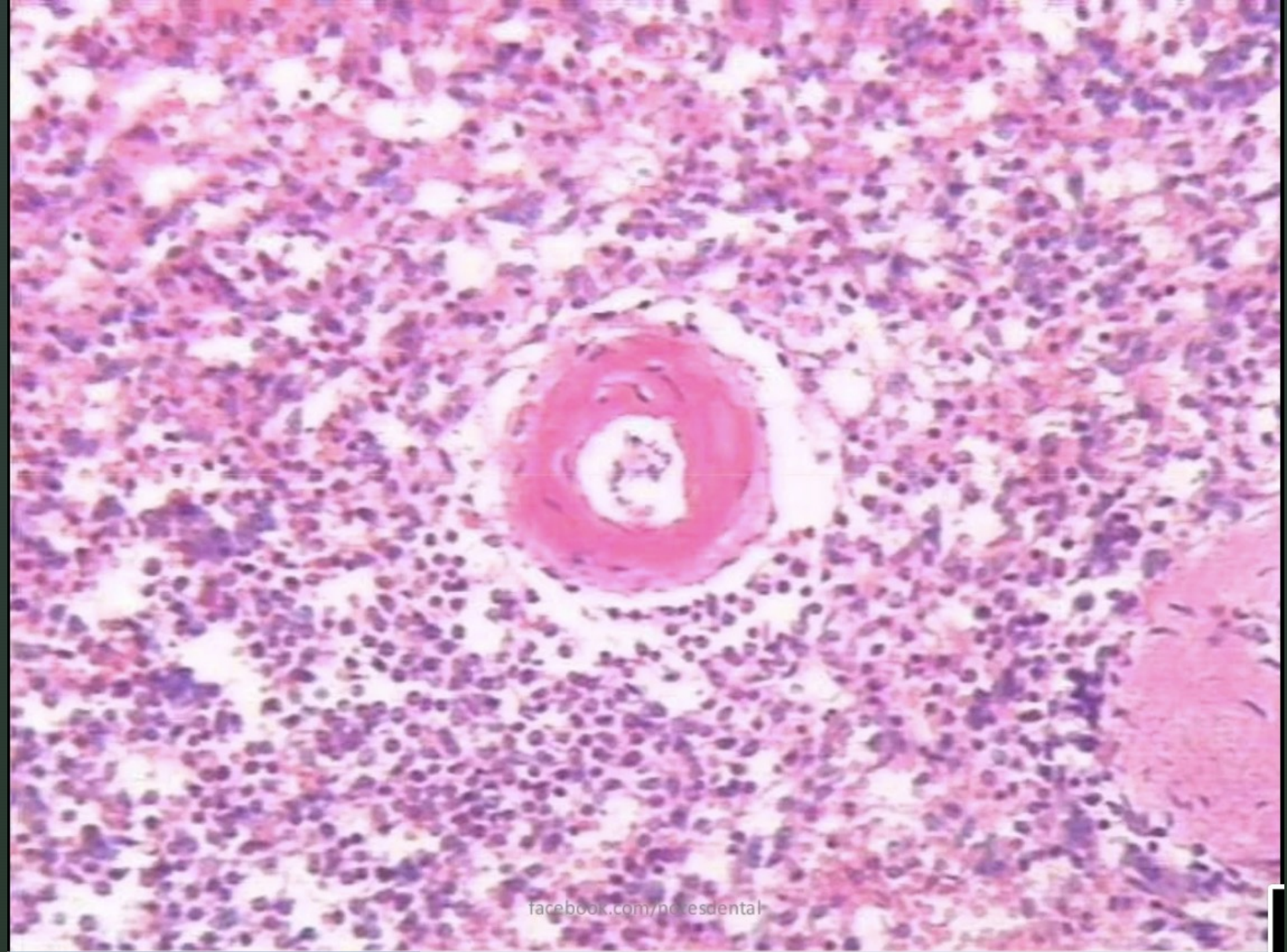
EXTRACELLULAR HYALINE

- Extracellular hyaline is seen in connective tissues.
- A few examples of extracellular hyaline change are as under:
  - **Hyaline degeneration** in ***leiomyomas*** of the uterus
  - **Hyalinised *old scar*** of fibro-collagenous tissues.
  - ***Hyaline arteriolosclerosis*** in renal vessels in hypertension and diabetes mellitus.
  - **Hyalinised glomeruli** in ***chronic glomerulonephritis***.
  - ***Corpora amylacea*** are rounded masses of concentric hyaline laminae seen in the **prostate** in the elderly, in the **brain** and in the **spinal cord** in old age, and in **old infarcts** of the lung.

Extracellular Hyaline



Extracellular hyaline deposit in leiomyoma uterus. The centres of whorls of smooth muscle and connective tissue show pink homogeneous hyaline material (connective tissue hyaline)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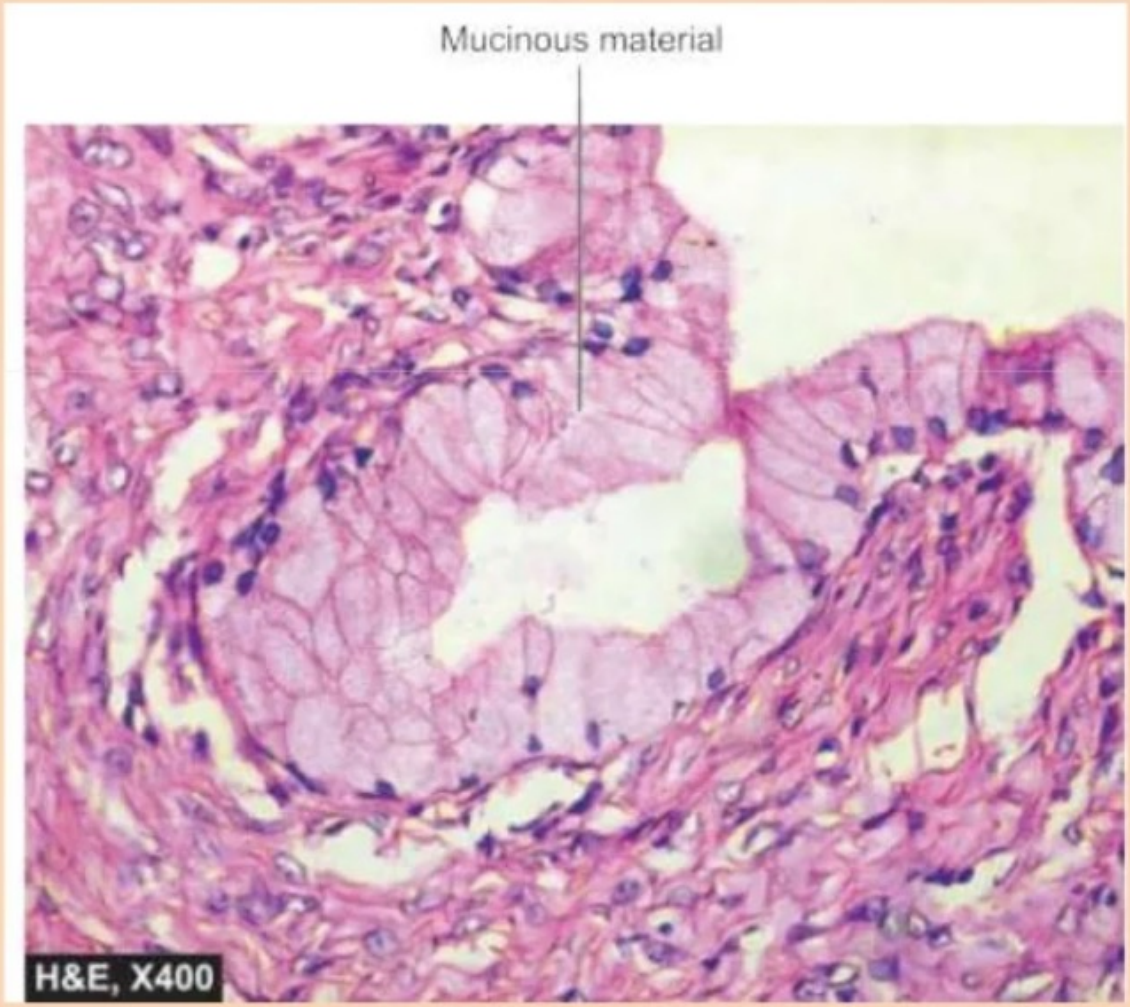
Mucoid degeneration

- Mucus containing **mucin (glycoprotein)** secreted by mucous glands.
- In certain cellular injur, there is change characterized by accumulation of **mucin** in intracellular or extracellular loci.
- Epithelial
  - composed of sialomucin plus neutral mucopolysaccharide.
  - May accumulate in intracellular or extracellular (if secreted) locations.
- Connective tissue
  - predominantly acid mucopolysaccharide, sulfated or carboxylated

EPITHELIAL MUCIN

- Following are some examples of functional excess of epithelial mucin:
- **Catarrhal inflammation** of mucous membrane (e.g. of respiratory tract, alimentary tract, uterus).
- **Obstruction of duct** leading to **mucocele** in the oral cavity and gallbladder.
- **Cystic fibrosis** of the **pancreas**.
- **Mucin-secreting tumours** (e.g. of ovary, stomach, large bowel etc)

Epithelial mucin

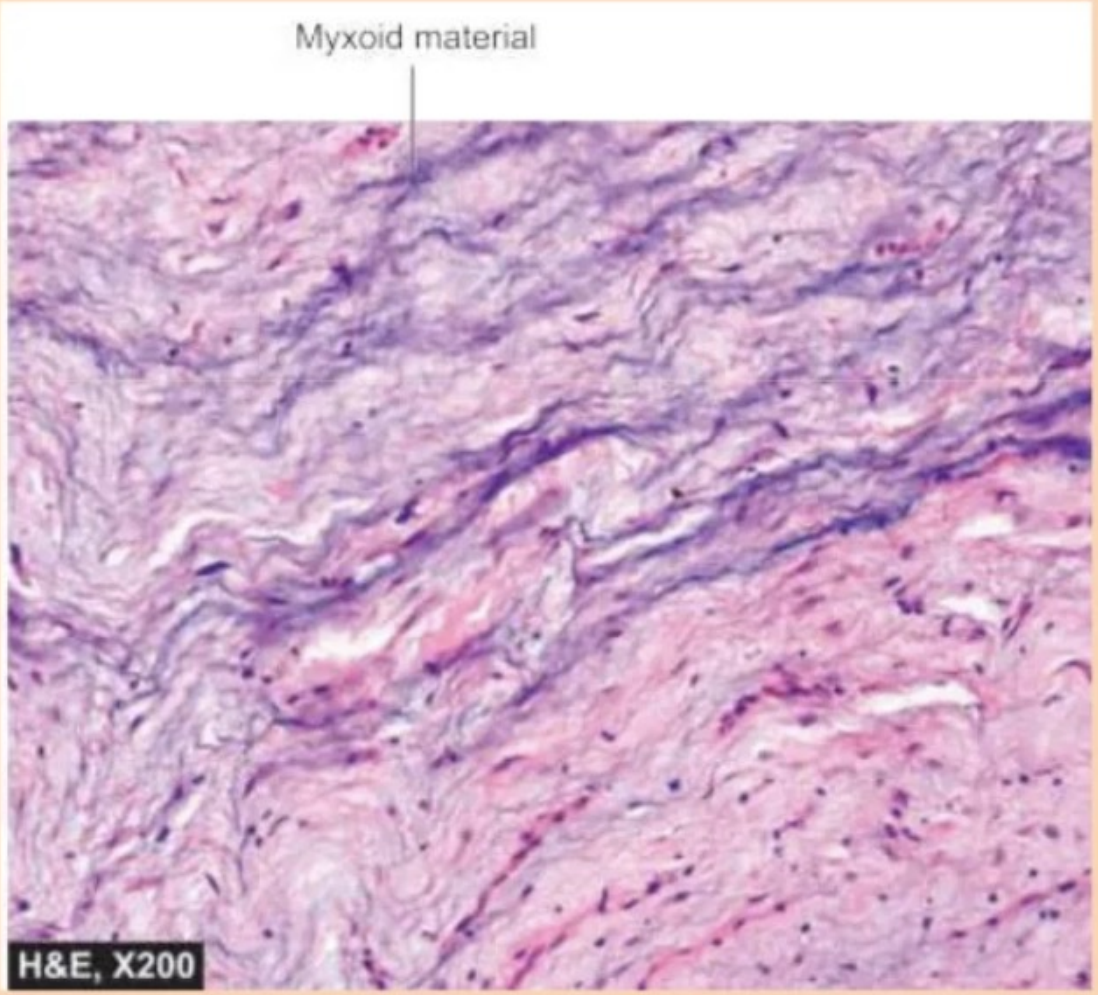


Mucinous cystadenoma of the ovary showing intracytoplasmic mucinous material in the epithelial cells lining the cyst

CONNECTIVE TISSUE MUCIN

- A few examples of disturbances of connective tissue mucin are as under
  - **Mucoid or myxoid degeneration** in some tumours e.g. myxomas, neurofibromas, fibroadenoma, soft tissue sarcomas etc
  - **Dissecting aneurysm** of the aorta due to **Erdheim's medial degeneration** and **Marfan's syndrome**.
  - **Myxomatous** change in the dermis in **myxoedema**.
  - **Myxoid** change in the **synovium in ganglion** on the **wris**

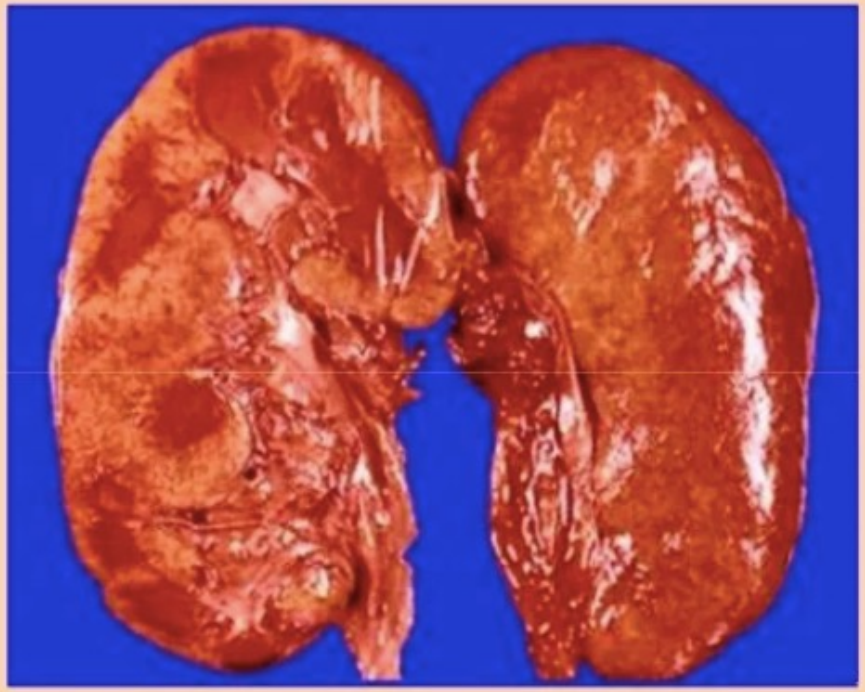
Connective tissue mucin



Myxoid change in neurofibroma

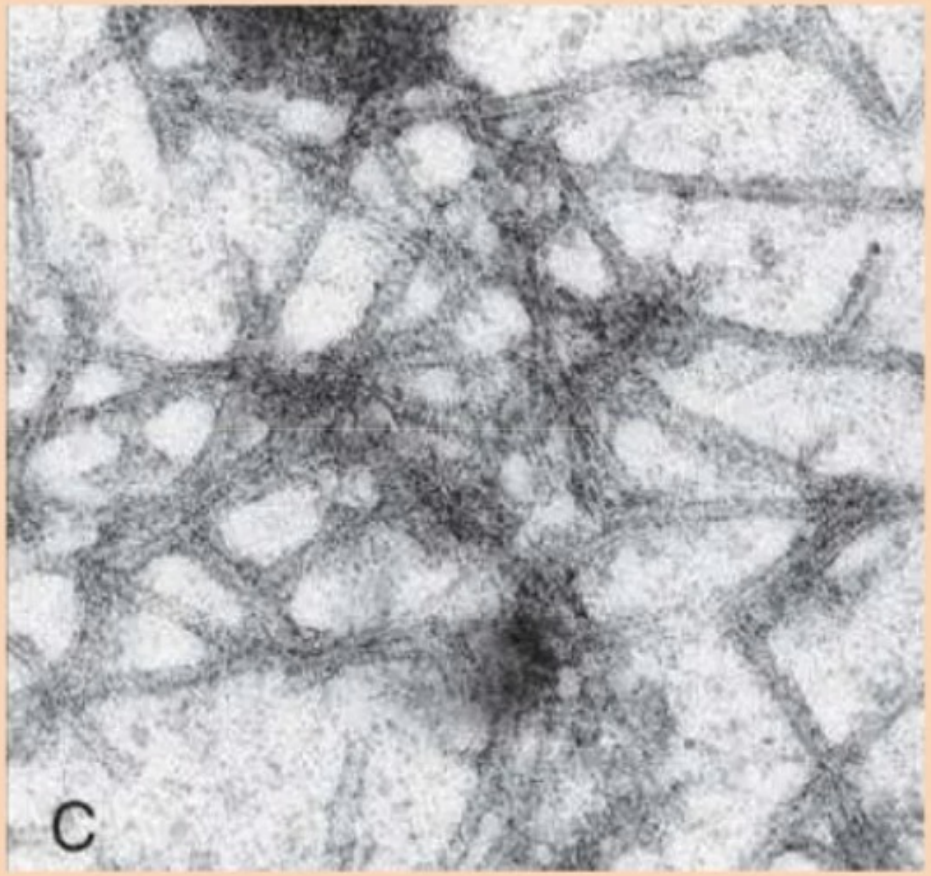
Amyloid degeneration

- Extracellular deposition of fibrillar proteinaceous substance called **amyloid**
  - a 'waxy substance' composed essentially of an abnormal protein
  - Particularly around the supporting fibres of blood vessels and basement membranes.
- Associated with a number of **inherited** and **inflammatory disorders**

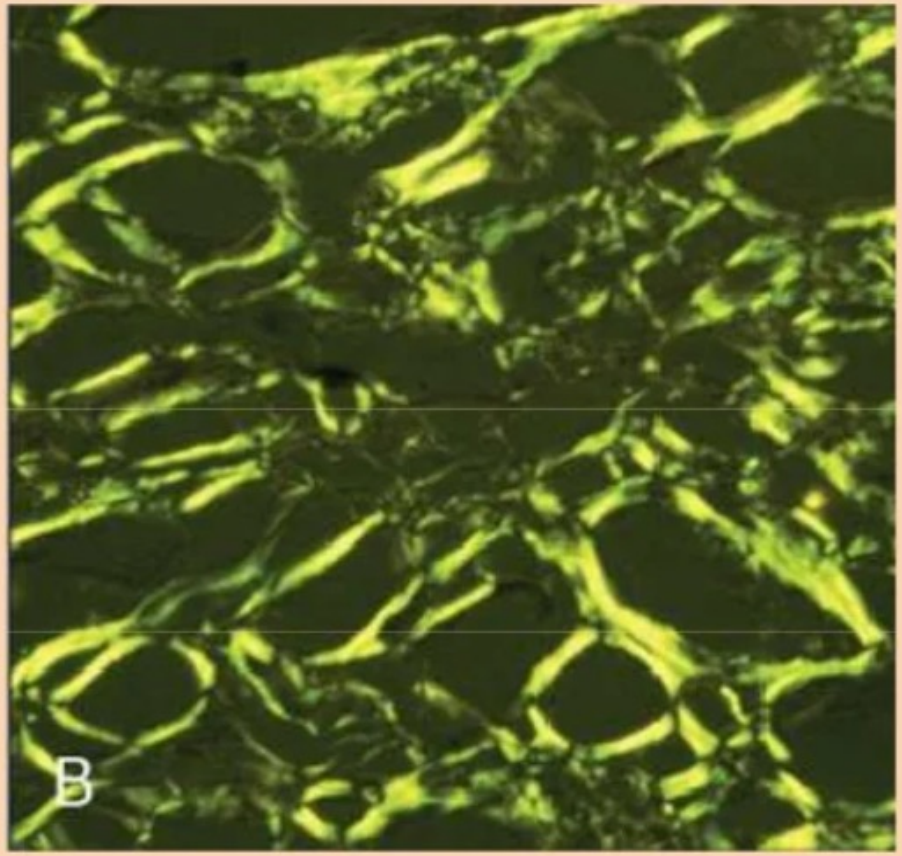


Primary Amyloidosis of kidneys

Structure of Amyloid



Electron micrograph of 7.5-10 nm amyloid fibrils.



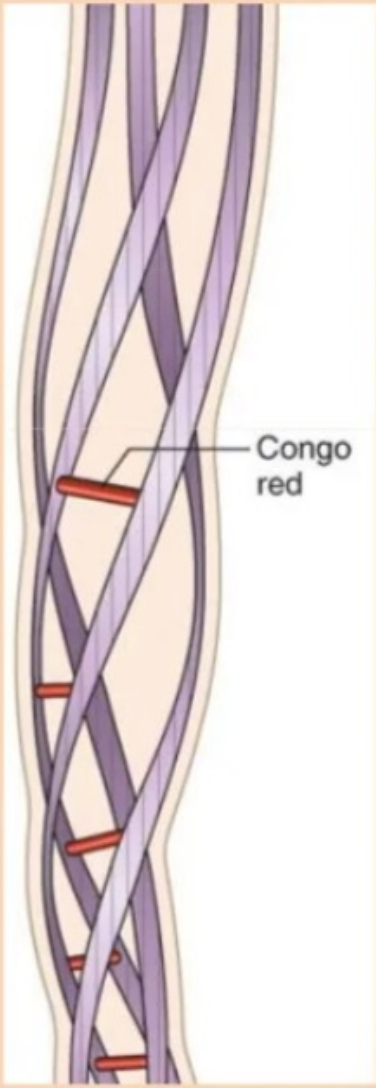
Congo red staining shows an apple-green birefringence under polarized light, a diagnostic feature of amyloid.

Types of Amyloid

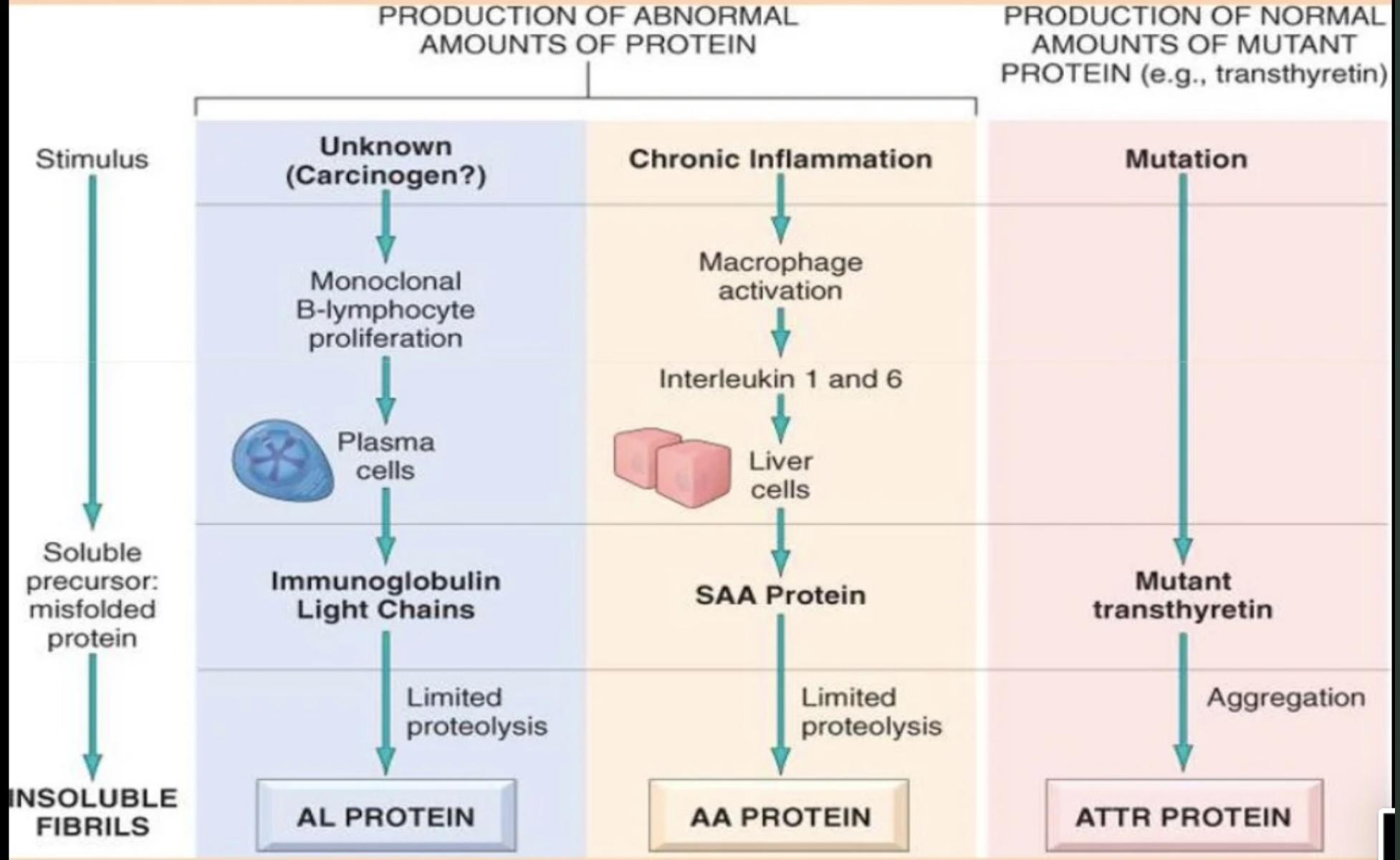
- Based on the biochemical analysis, its composed of 2 main types of complex proteins.
- **Fibril proteins:** comprise about 95% of amyloid.
  - AL (amyloid light chain) protein
  - AA (amyloid associated) protein
  - Other proteins (**Transthyretin (TTR), Aβ2-microglobulin (Aβ2M), β-amyloid protein (Aβ), Immunoglobulin heavy chain amyloid (AH))**
- **Non-fibrillar components:** which include *P-component* predominantly; constitute the remaining 5% of amyloid
  - **Amyloid P (AP)-component**
  - **Apolipoprotein-E (apoE)**
  - **α-1 anti-chymotrypsin.**
  - **Protein X.**

PATHOGENESIS OF AMYLOIDOSIS

- Result of immunologic mechanisms.
- Multifactorial and that different mechanisms are involved in different types of **amyloid**.
- Fundamentally a **disorder** of **protein misfolding**.
- More than 20 (at last count, 23) different proteins can aggregate and form fibrils with the appearance of amyloid
- The dye Congo red binds to these fibrils and produces a red-green **dichroism** (**birefringence**)
  - commonly used to identify amyloid desposits in tissues



PATHOGENESIS OF AMYLOIDOSIS



CLASSIFICATION OF AMYLOIDOSIS

- **Based on cause**
  - **Primary :** with unknown cause and the deposition is in the disease itself
  - **Secondary:** as a complication of some underlying known disease
- **Based on extent of amyloid deposition**
  - ***Systemic (generalised)*** involving multiple organs
  - ***Localised amyloidosis*** involving one or two organs or sites
- **Based on histological basis**
  - **Pericollagenous***:* corresponding in distribution to primary amyloidosis
  - **Perireticulin:** corresponding in distribution to secondary amyloidosis

CLASSIFICATION OF AMYLOIDOSIS

- **Based on clinical location**,
  - **Pattern I:** involving tongue, heart, bowel, skeletal and smooth muscle, skin and nerves),
  - **Pattern II*:*** principally involving liver, spleen, kidney and adrenals
  - **Mixed pattern :** involving sites of both pattern I and II
- **Based on tissues** in which amyloid is deposited,
  - **Mesenchymal :** organs derived from mesoderm
  - **Parenchymal:** organs derived from ectoderm and endoderm
- **Based on precursor biochemical proteins**, into specific type of serum amyloid proteins.

CLASSIFICATION OF AMYLOIDOSIS

Category	Associated Disease	Biochemical Type	Organs Commonly Involved
A. SYSTEMIC (GENERALISED) AMYLOIDOSIS			
1. *Primary*	Plasma cell dyscrasias	AL type	Heart, bowel, skin, nerves, kidney
2. *Secondary (Reactive)*	Chronic inflammation, cancers	AA type	Liver, spleen, kidneys, adrenals
3. *Haemodialysis-associated*	Chronic renal failure	$A\beta_2M$	Synovium, joints, tendon sheaths
4. *Heredofamilial*			
i. *Hereditary polyneuropathies*	—	ATTR	Peripheral and autonomic nerves, heart
ii. *Familial Mediterranean fever*	—	AA type	Liver, spleen, kidneys, adrenals
iii. *Rare hereditary forms*	—	AApoAI, AGel ALys, AFib, ACys	Systemic amyloidosis
B. LOCALISED AMYLOIDOSIS			
1. *Senile cardiac*	Senility	ATTR	Heart
2. *Senile cerebral*	Alzheimer's, transmissible encephalopathy	Aβ, APrP	Cerebral vessels, plaques, neurofibrillary tangles
3. *Endocrine*	Medullary carcinoma type 2 diabetes mellitus	Procalcitonin Proinsulin	Thyroid Islets of Langerhans
4. *Tumour-forming*	Lungs, larynx, skin, urinary bladder, tongue, eye	AL	Respective anatomic location

(AL= Amyloid light chain; AA= Amyloid-associated protein; Aβ2M= Amyloid β2-microglobulin; ATTR= Amyloid transthyretin; APrP=Amyloid of prion proteins, Aβ= β-amyloid protein).

STAINING CHARACTERISTICS OF AMYLOID

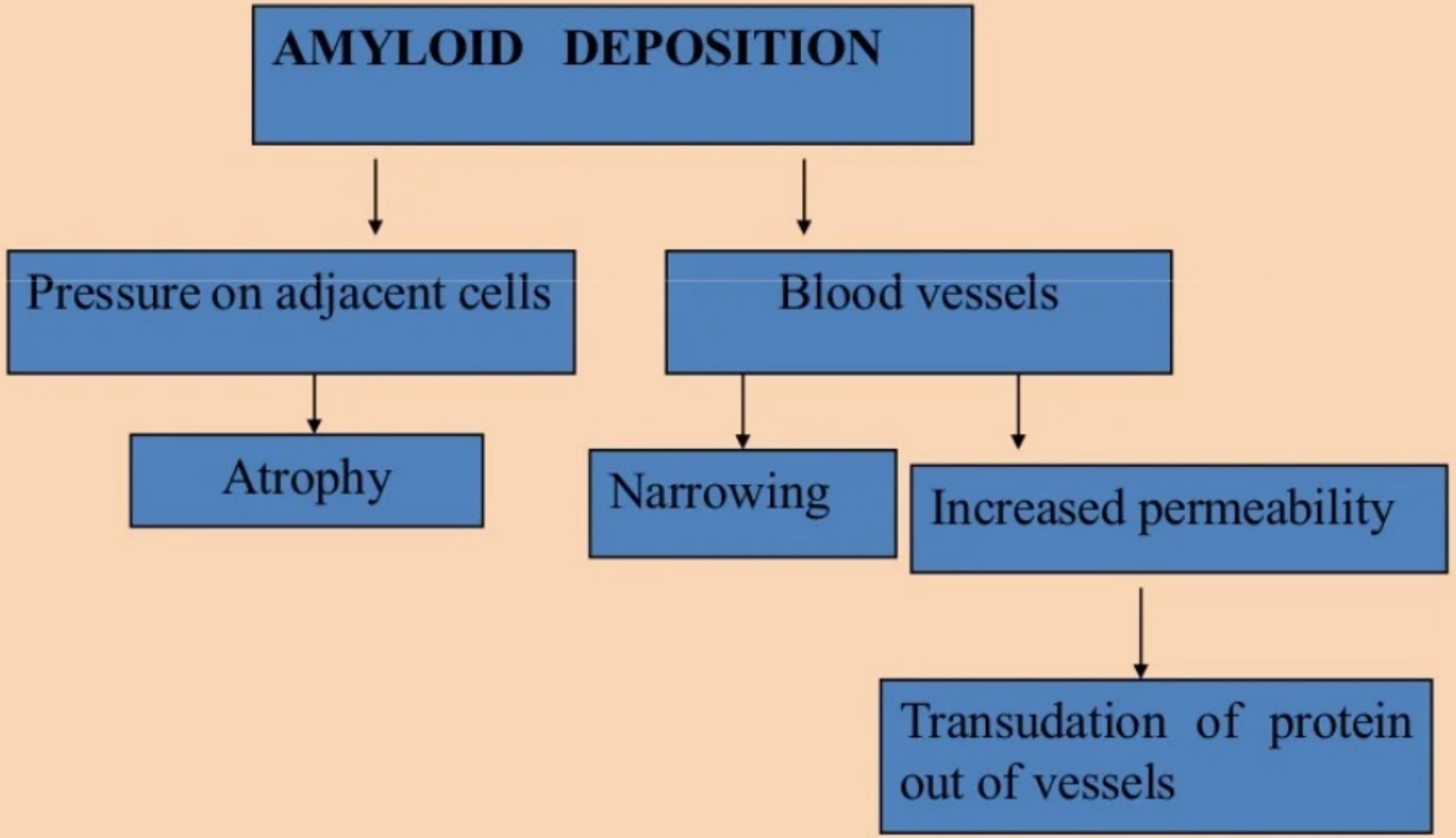
- **STAIN ON GROSS**
  - Virchow
  - frozen/paraffin section
  - Lugol's iodine imparts ***mahogany brown*** colour to the amyloid
  - on addition of dilute sulfuric acid turns **blue**.
- **H & E**
  - extracellular, homogeneous, structureless
  - Eosinophilic hyaline material, especially in relation to blood vessels

Stain	Appearance
1. *H & E*	Pink, hyaline, homogeneous
2. *Methyl violet/Crystal violet*	Metachromasia: rose-pink
3. *Congo red*	Light microscopy: pink-red Polarising light: red-green birefringence
4. *Thioflavin-T/Thioflavin-S*	Ultraviolet light: fluorescence
5. *Immunohistochemistry (antibody against fibril protein)*	Immunoreactivity: Positive
6. *Non-specific stains:*	
i) Standard toluidine blue	Orthochromatic blue, polarising ME dark red
ii) Alcian blue	Blue-green
iii) PAS	Pink

DIAGNOSIS OF AMYLOIDOSIS

- **BIOPSY EXAMINATION:** commonest and confirmatory method for diagnosis in a suspected case of amyloidosis.
- **IN VIVO CONGO RED TEST:** confirmatory
- **OTHER TESTS**
  - supportive of amyloid disease
  - electrophoresis, immunoelectrophoresis of urine and serum, and bone marrow aspiration

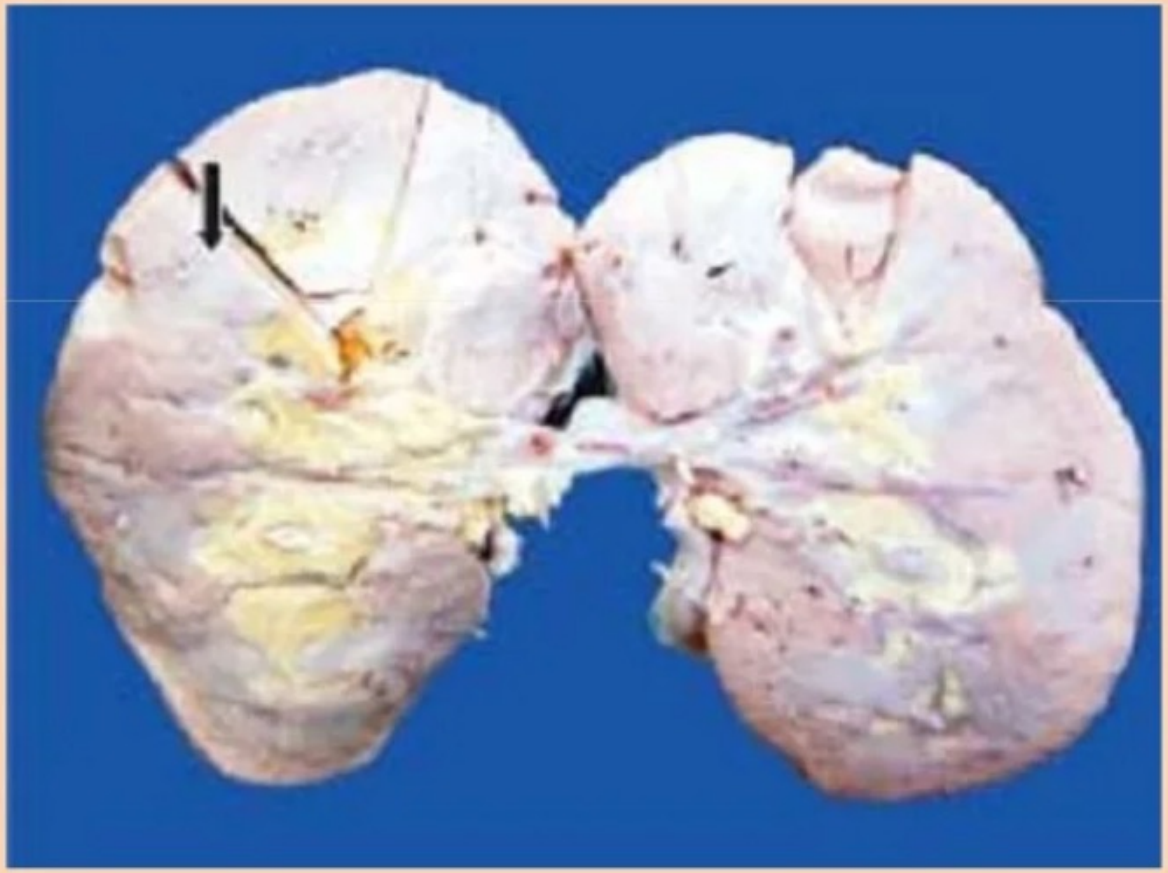
Pathological effects of Amyloidosis



MORPHOLOGIC FEATURES OF AMYLOIDOSIS OF ORGANS

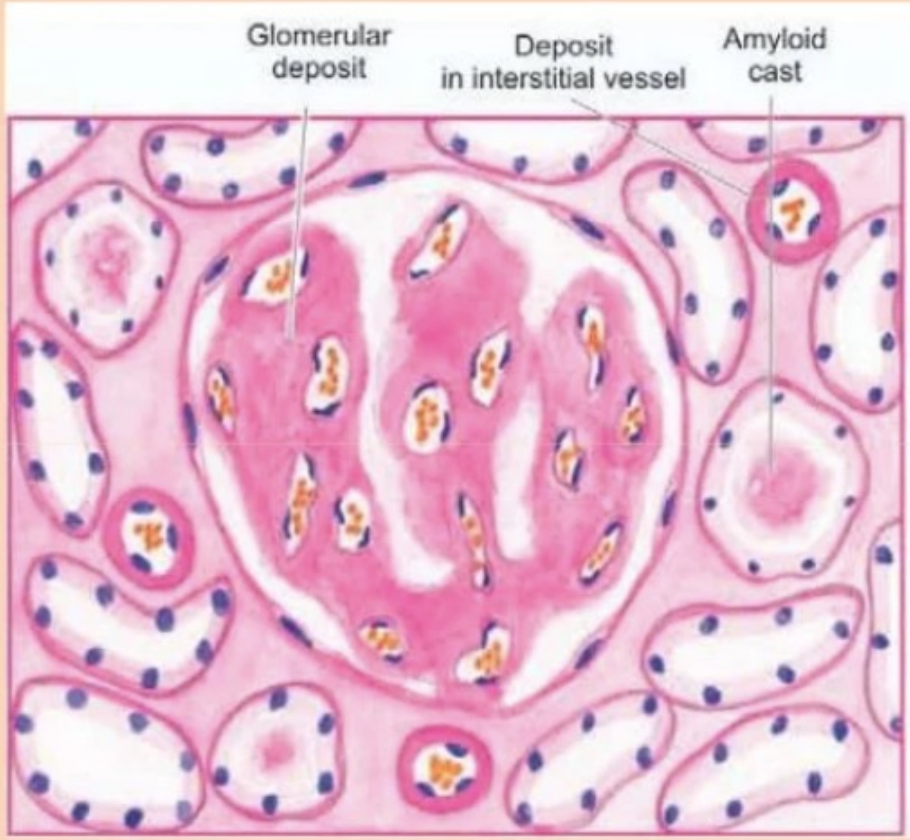
- Different organs shows variation in morphologic pattern, some features are applicable in general to most of the involved organs
- Most commonly amyloid deposits appear at the contacts between the vascular spaces and parenchymal cells
- **Grossly**
  - affected organ is usually enlarged, pale and rubbery
  - Cut surface shows firm, waxy and translucent parenchyma
  - positive staining with the iodine test.
- **Microscopically**
  - the deposits of amyloid are found in the extracellular locations, initially in the walls of small blood vessels producing microscopic changes and effects,
  - the deposits are in large amounts causing macroscopic changes and effects of pressure atrophy.

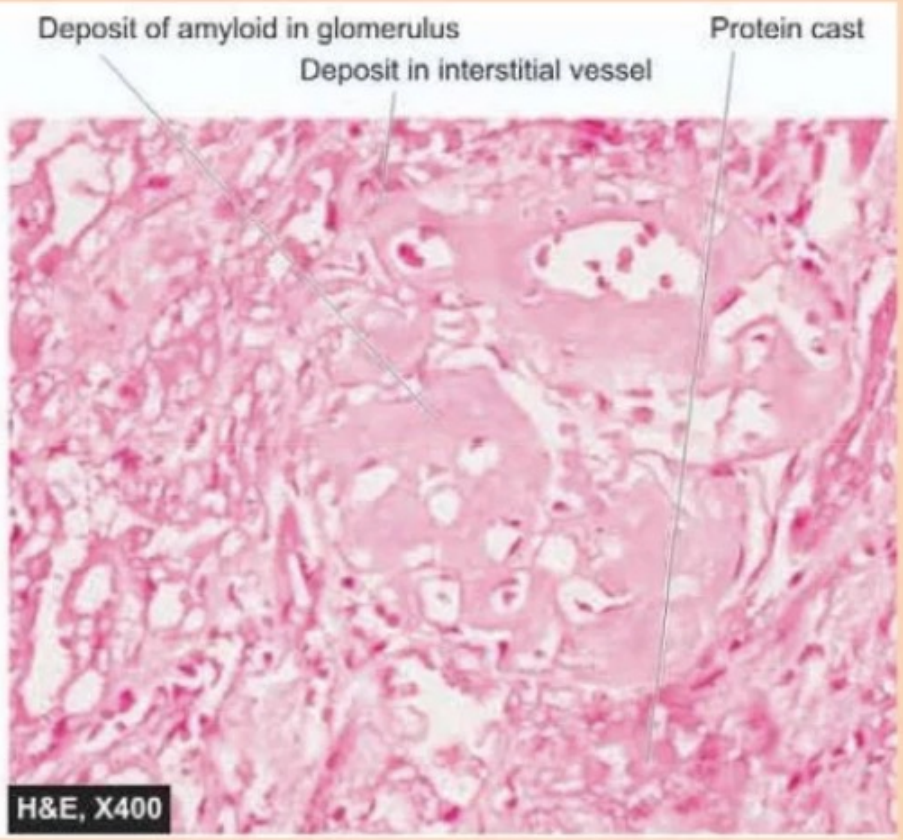
Amyloidosis of kidney



The kidney is small and pale in colour. Sectioned surface shows loss of cortico-medullary distinction (arrow) and pale, waxy translucency.

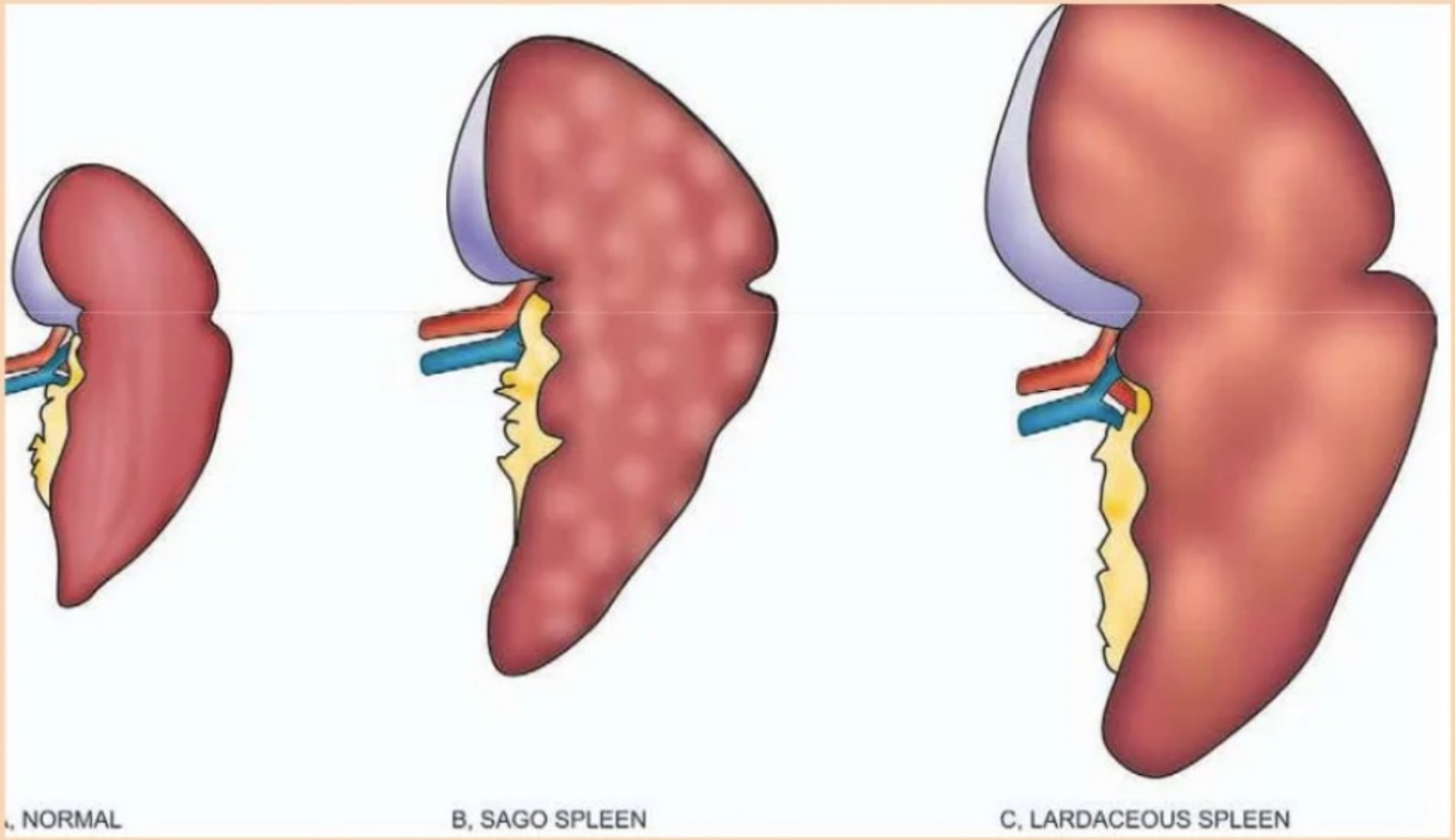
Amyloidosis of kidney



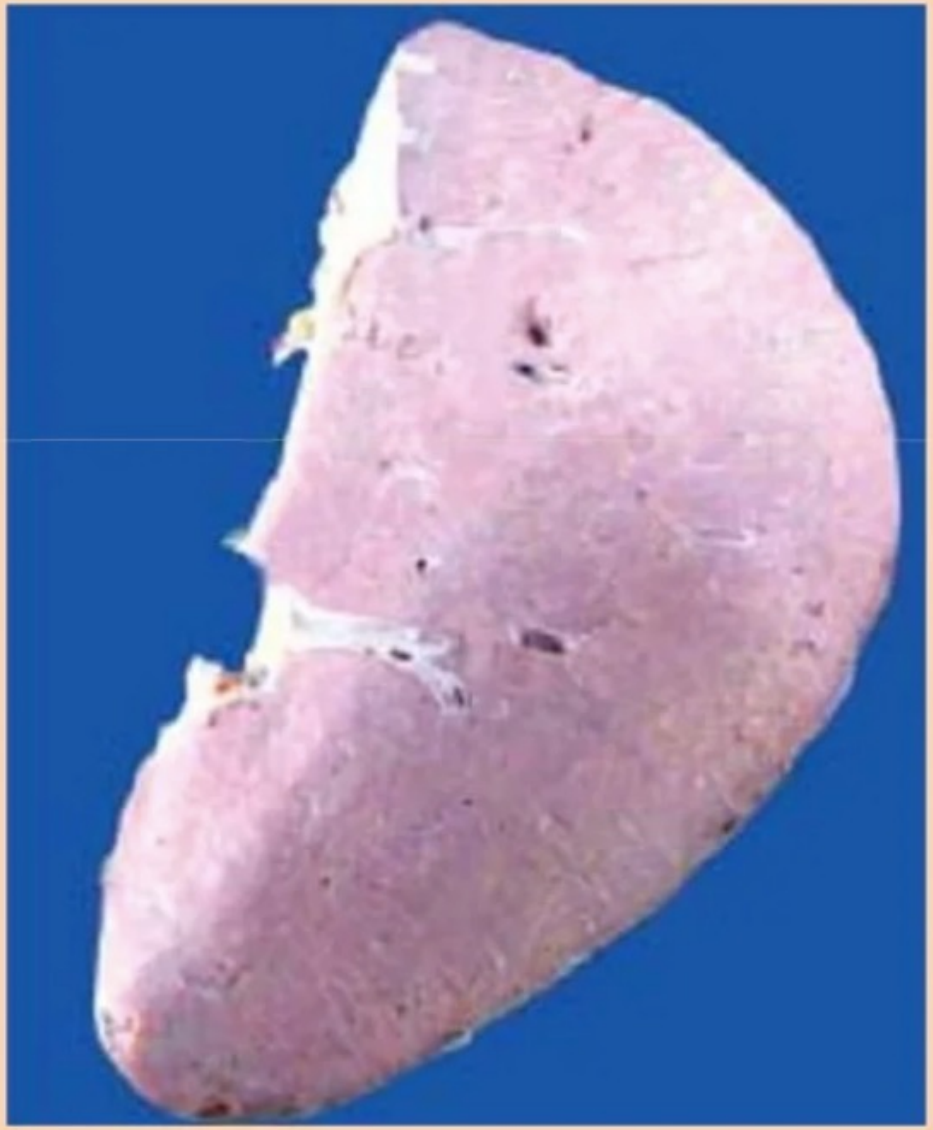


The amyloid deposits are seen mainly in the glomerular capillary tuft. The deposits are also present in peritubular connective tissue producing atrophic tubules and amyloid casts in the tubular lumina, and in the arterial wall producing luminal narrowing.

Amyloidosis of the spleen

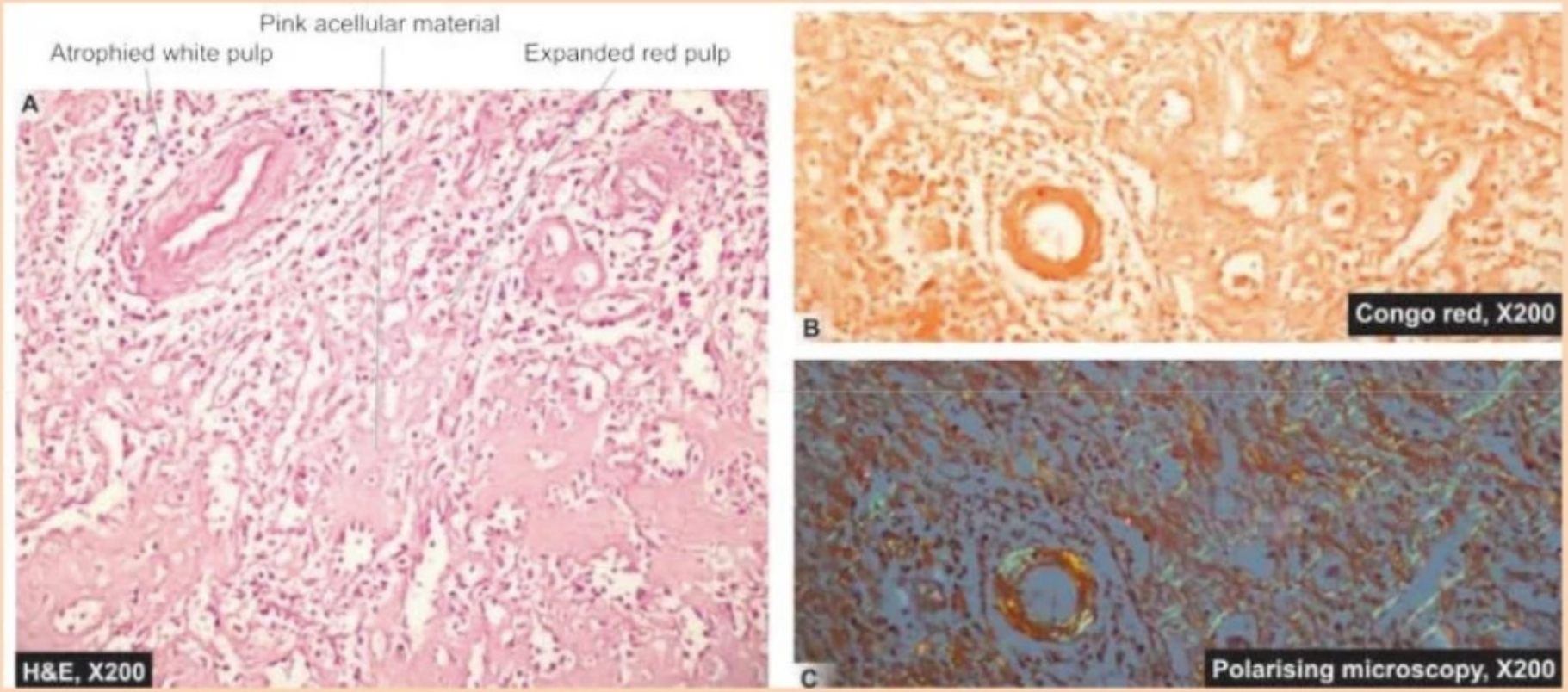


Lardaceous amyloidosis of the spleen



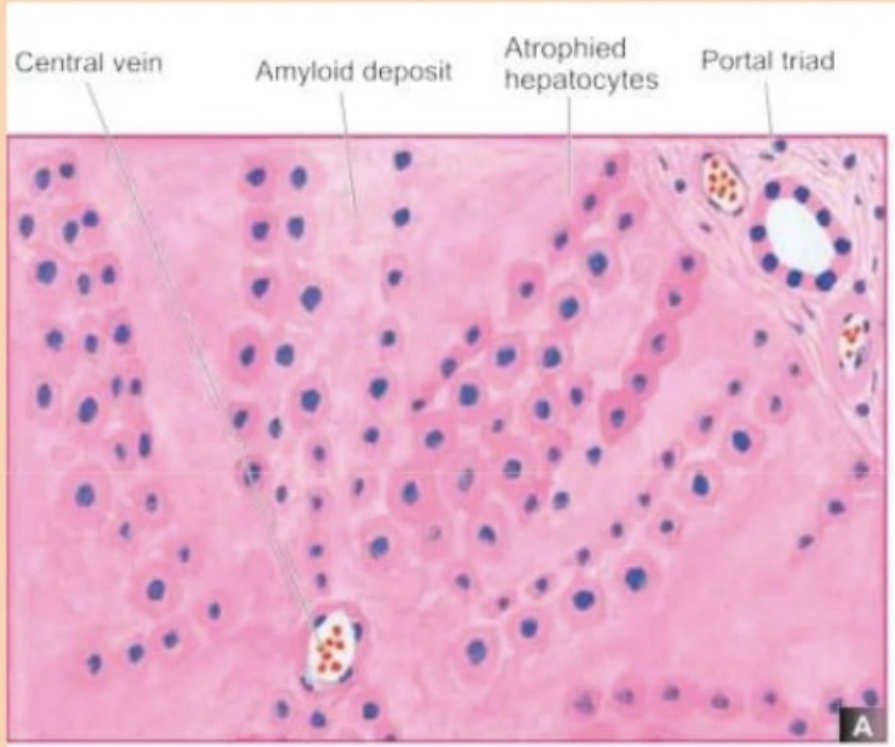
The sectioned surface shows presence of plae waxy translucency in a map-like pattern

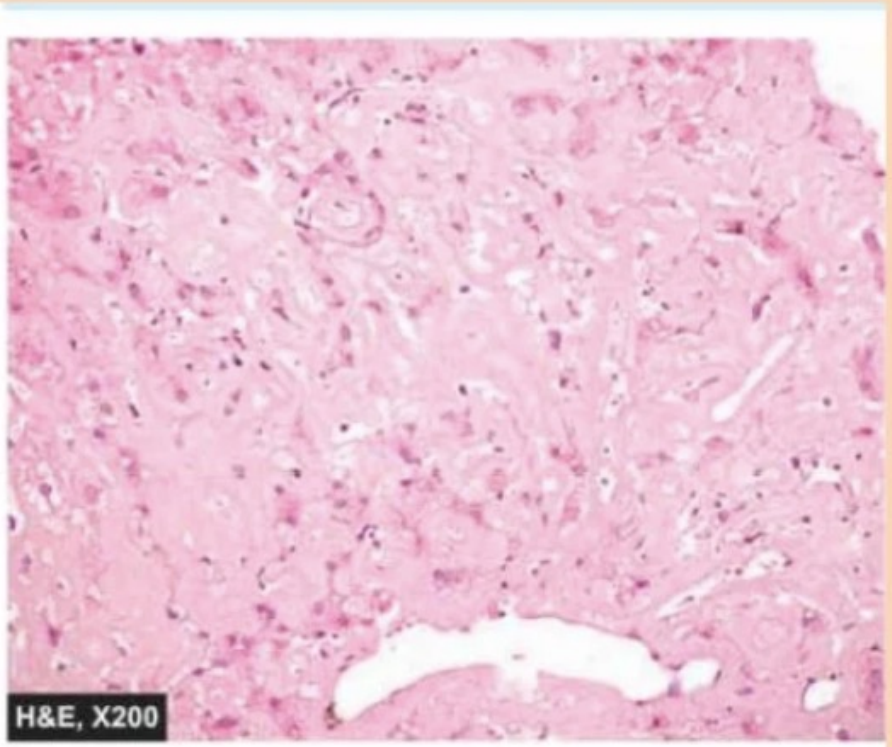
Amyloidosis spleen

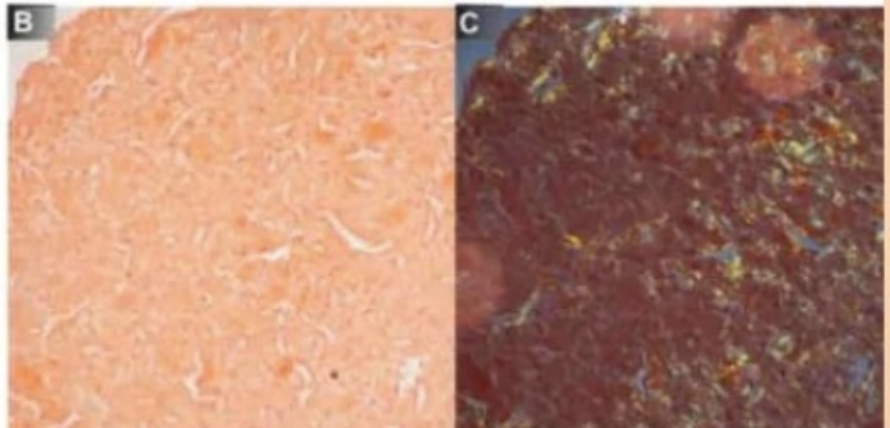


A, The pink acellular amyloid material is seen in the red pulp causing atrophy of while pulp.
B, Congo red staining shows Congophilia as seen by red-pink colour.
C, When viewed under polarising microscopy the corresponding area shows apple-green birefringence.

Amyloidosis of the liver







A, The deposition is extensive in the space of Disse causing compression and pressure atrophy of hepatocytes.
B, Congo red staining shows congophilia which under polarising microscopy.
C, shows apple-green birefringence.

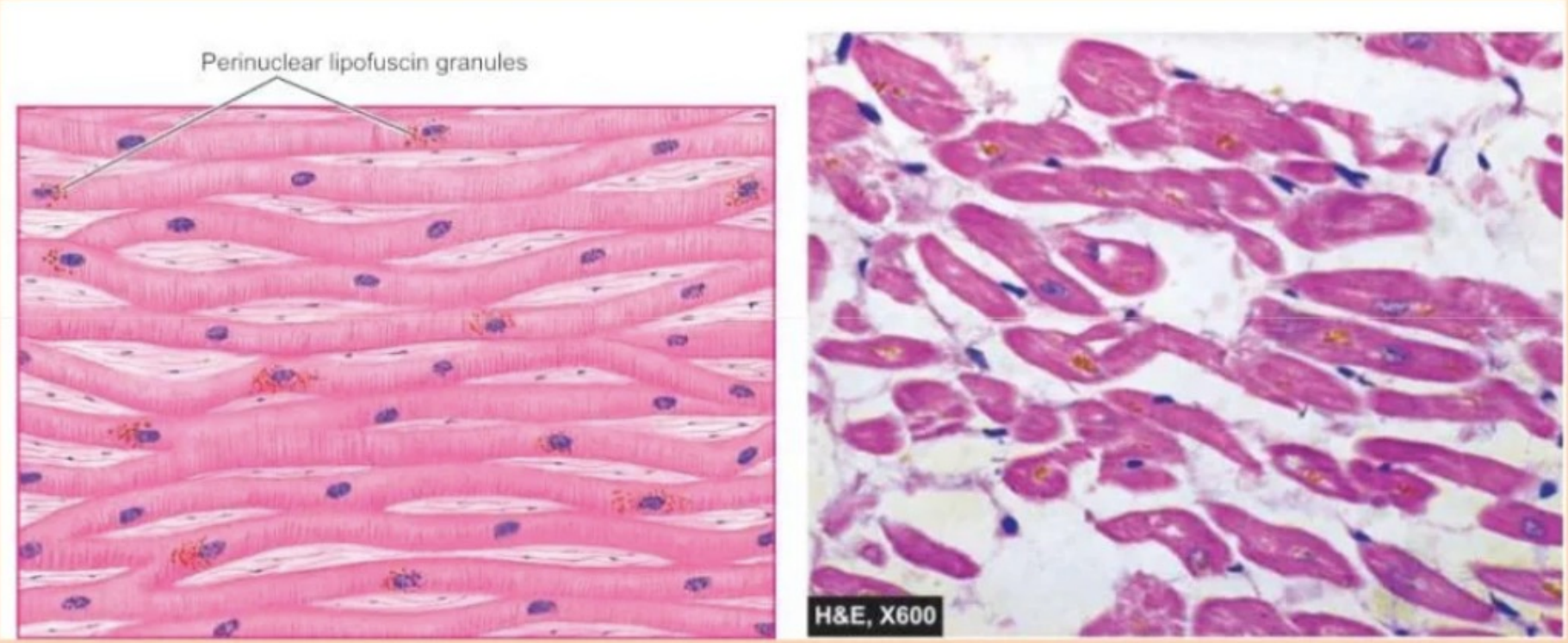
Pathologic Pigments

- Pigments are coloured substances present in most living beings including humans.
- There are 2 broad categories of pigments: **endogenous and exogenous.**

Endogenous Pigmentation

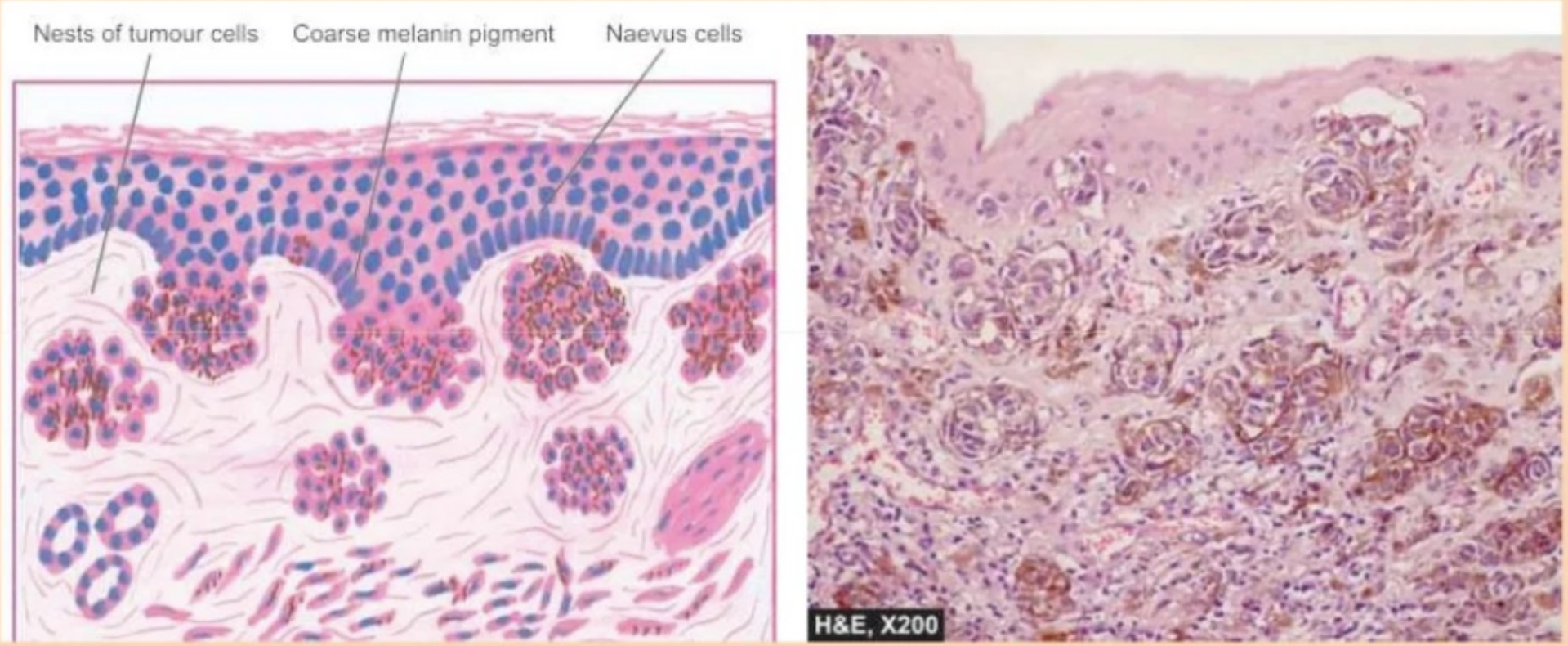
- **Melanin**
  - **Generalised hyperpigmentation:** *Addison's disease, Chloasma, chronic arsenical poisoning*
  - **Focal hyperpigmentation:** *Cäfe-au-lait spots, Peutz-Jeghers syndrome, Melanosis coli, Melanotic tumours, Lentigo , Dermatopathic lymphadenitis*
  - **Generalised hypopigmentation:** *Albinism*
  - **Localised hypopigmentation:** *Leucoderma, Vitiligo , Acquired focal hypopigmentation,* leprosy, healing of wounds, DLE, radiation dermatitis
- **Melanin-like pigment**
  - Alkaptonuria
  - Dubin-Johnson syndrome
- **Haemoprotein-derived pigments**
  - Haemosiderin
  - Acid haematin (Haemozoin)
  - Bilirubin
  - Porphyrins
- **Lipofuscin (Wear and tear pigment)**

Endogenous Pigmentation



Brown atrophy of the heart. The lipofuscin pigment granules are seen in the cytoplasm of the myocardial fibres, especially around the nuclei.

Endogenous Pigmentation

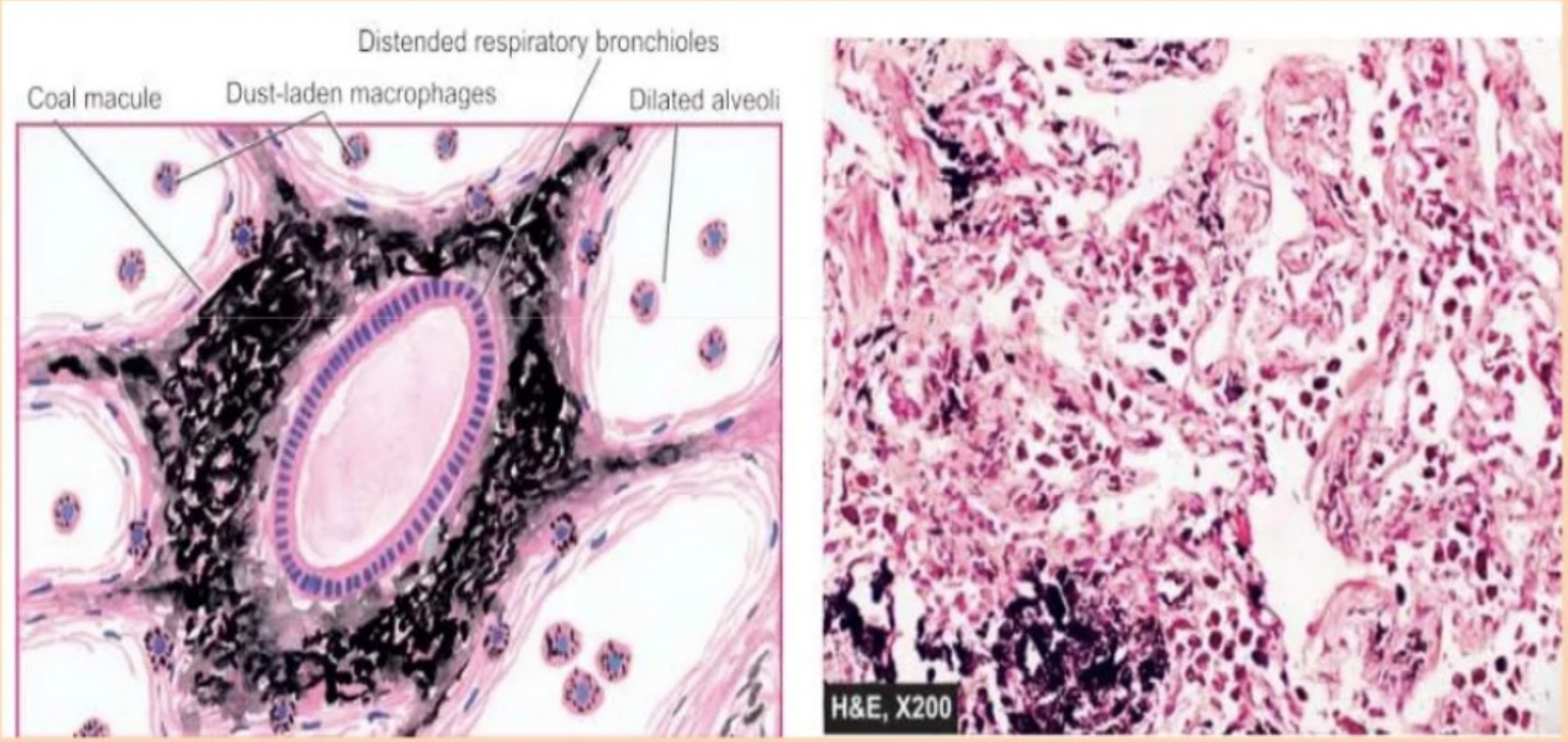


Compound naevus showing clusters of benign naevus cells in the dermis as well as in lower epidermis. These cells contain coarse, granular, brown-black melanin pigment

EXOGENOUS PIGMENTS

- **Inhaled pigments**
  - Atmospheric pollutants and of smokers
  - **Pneumoconiosis**: occupational lung diseases
  - ***Anthracosis****:* deposition of coal
- **Ingested pigments**
  - ***Argyria*** *:* silver compounds - brownish pigmentation in the skin, bowel, and kidney.
  - ***Burtonian Lines****: Chronic lead poisoning* - blue lines on teeth at the gumline.
  - ***Melanosis coli*** *:* cathartics (stimulates evacuation of the bowels)
  - ***Carotenaemia****:* yellowish-red colouration of the skin - ingestion of carrots which contain carotene.
- **Injected pigments (Tattooing)**: India ink, cinnabar and carbon deposited in dermis

EXOGENOUS PIGMENTS



Anthracosis lung: There is presence of abundant coarse black carbon pigment in the septal walls and around the bronchiole